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THE RELATION OF INTENSITY OF RADIUM RADIATIONS TO TISSUE REACTION USING A SEGMENT OF A GROWING MOUSE TAIL AS A BIOLOGICAL INDICATOR*

By HALSEY J. BAGG, Ph.D., *and* C. ROBERT HALTER, Ph.D.

Douglas Research Laboratory, Memorial Hospital, and Cornell University Medical College

NEW YORK CITY

WHEN a large intensity is coupled with a short period of exposure, or a small intensity is coupled with a long period of exposure, the resulting biological reactions of living tissues so treated may or may not be similar. In fact, among investigators working in this field one finds a wide divergence of opinion, and even when the same materials and methods are used, conclusions arrived at in various laboratories have been opposed.[1]

No doubt an explanation for this divergence of opinion may be found in the great variety of biological indicators that have been used, and in intrinsic factors of variation that occur normally in the tissues selected.

STATEMENT OF THE PROBLEM

We shall describe in this paper a series of experiments designed to test the validity of the so-called Bunsen-Roscoe Law (intensity × time = a constant) and have chosen a biological indicator which may be examined from day to day over a fairly long period of observation. The method employed gives an opportunity to judge rather closely the degree to which maximum tissue reaction may attain, as well as the intermediate steps that precede, and the reparative processes that follow the maximum reaction. We have used three radium applicators—the so-called radium bulb, both unfiltered and using 2 mm. brass filtration, and the platinum-gold tube giving a filtration of 0.5 mm. We have treated our tissues when the radon was near its maximum strength and then waited varying periods until the strength of the radon had decreased and then treated another series with the conditions as identical as possible except for the changes in the intensity of radiation. The problem then was to determine if a specified tissue reaction was essentially similar irrespective of whether the treatment was given by a high intensity, coupled with a short period of exposure, or a small intensity coupled with a long period of exposure.†

EXPERIMENTAL METHODS

In a previous article[2] we have fully described the methods employed when a seg-

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ment of a growing mouse tail is used as a biological indicator. For further details the reader is referred to that publication. Briefly the method is as follows: A young mouse, seven, eight or nine days of age, is fastened on a lead shield so that its tail protrudes from one edge while its body is well shielded from the radiation. The distal and proximal regions of the tail are also protected by lead, and only that portion of the tail is irradiated where its diameter is 1.5 mm. A large paraffin block is below the irradiated surface, and where the source of radiation is several millimeters above the tail, a paraffin block is placed between the irradiated surface and the source of radiation. The radiation is always applied to the dorsal surface of the tail.

EXPERIMENTAL RESULTS

1. *The glass radon bulb placed directly on the dorsal surface of the tail.*

In Tables I, II and III we have given the summary of results for these treatments. The data are in pairs of treatments in serial arrangement according to the ratios of intensities. The dosage is given in millicurie-minutes and the strength of the bulbs in millicuries. In order to simplify the tables, the time of treatment is not recorded, but this may be easily computed from the data given. The tables show that each of a pair of two animals is given the same number of millicurie-minutes, the first in the series receiving the dose from a radon bulb when strong, and the second animal receiving the same number of millicurie-minutes from the same bulb when its strength had decreased. It is important to note that these data are compiled from treatments given by various radon bulbs recorded below.* The bulbs vary slightly in the thickness of the glass wall and in certain instances there were very small drops of mercury within the bulbs themselves. The mercury was inadvertently included when the bulb was detached from the radon collecting apparatus. An increase in the thickness of the glass and the presence of mercury within the applicator tends to decrease the resulting severity of tissue reaction. One therefore should not compare the tissue reactions for the same dosage as given by different bulbs without bearing these factors in mind. The conditions just mentioned do not interfere with a comparison of treatments made by the same bulb.

In the last two columns of the tables are presented the initial and intermediate tissue reactions and the final reactions respectively. In gauging the results we are measuring qualitive and not quantative changes as shown in the tissues. For simplicity of recording we have indicated the changes in percentages. These must be considered as representing estimated changes only. A very slight, slight, moderate and complete epilation are recorded as 5 per cent, 10 per cent, 50 per cent and 100 per cent epilation respectively.

Let us consider the results of the first experiment shown in Table I. Animal No. 637 was treated with 515 mc. for three seconds, the dose being 25 millicurie-minutes. This was a relatively small dose and the first noticeable change was a very slight epilation (5 per cent) on the dorsal surface of the tail on the 22d day post-treatment. The epilation was in the immediate vicinity of the treated area. The epilation increased to moderate by the 27th day and at the 35th day, when the observations were terminated, the epilation had increased to approximately 70 per cent. Animal No. 710 was the same age when treated and received a similar dose when the same bulb had decreased in strength to 0.6 mc. (as estimated by the tables of the Radium Chemical Company which are based on the work of Kolowrat and Failla). The time of treatment was 44.6 minutes. The ratio of intensities was 920:1. The initial reaction was noted somewhat earlier than in the previous instance, but on the whole the resulting effect was apparently essentially similar.

* Bulbs identified as E, I., etc. Numbers indicate catalogue numbers of animals. E=108, 131; J=167, 219-23, 282-3; I.=314, 321, 337, 361, 388,478; Q=400-3, 419-20, 422-5, 427; V=426, 477-9, 480-2, 529-32, 496, 499, 434-6; W=545, 577; X=582-3, 608, 612; Y=298, 363, 595-8, 618-20, 623-26, 628, 658-9, 662-3, 665; Z=632, 636, 637, 702, 709, 710.

Table 1 shows the results of treating 74 animals with ratios of intensities varying from 920:1 to 9:1. In all these treatments we have noted no significant tendency for a swing of the results in one direction or the other. In other words, we find that under the present experimental conditions, the Bunsen-Roscoe Law is apparently substantiated.

Eight more pairs of treatments were given by the same methods, but for the sake of convenience in discussion they are

Table I

Ratios of Intensity	Animal No.	Dosage mc-min.	No. mc.	Tissue Reaction	
				Initial Reactions and Time of Appearance in Days	Final Reaction at 35th Day Post-Treatment
920:1	637	25	515	5% dorsal epilation.....22d. 50% dorsal epilation.....27d.	70% dorsal epilation
	710	25	0.6	10% dorsal epilation.....13d. 90% dorsal epilation....21–23d.	80% dorsal epilation
554:1	636	50	515	10% dorsal epilation.....19d. 100% dorsal epilation.....27d.	100% dorsal epilation
	709	50	0.9	5% dorsal epilation..... 9d. 50% annular epilation.....10d.	100% dorsal epilation
456:1	632	200	515	10% dorsal epilation..... 7d. 100% annular epilation.....14d. constriction.....17d.	100% annular epilation
	702	200	1.1	10% dorsal epilation..... 7d. 100% annular epilation with constriction.....17d.	Spontaneous amputation, 23d.
181:1	314	250	221	10% dorsal epilation..... 8d. 50% annular epilation.....11d. constriction.....18d.	100% annular epilation
	388	250	1.2	10% dorsal epilation..... 7d. 10% annular epilation.....12d.	100% annular epilation
160:1	219	150	384	10% annular epilation..... 7d. constriction.....13d.	100% annular epilation with constriction
	282	150	2.4	10% dorsal epilation.....15d. 100% dor., 10% vent. epil....20d.	100% annular epilation
150:1	221	150	384	10% dorsal epilation.....10d. 100% annular epilation.....12d. constriction.....13d.	100% annular epilation
	283	150	2.5	10% annular epilation..... 9d. 100% annular epilation with constriction.....13d.	100% annular epilation
108:1	298	102	555	10% annular epilation.....11d.	100% dorsal epilation
	363	102	5.1	10% dorsal epilation.....11d.	100% dorsal epilation

TABLE I (*Cont.*)

Ratios of Intensity	Animal No.	Dosage mc-min.	No. mc.	Tissue Reaction	
				Initial Reactions and Time of Appearance in Days	Final Reaction at 35th Day Post-Treatment
105:1	597	200	524	10% dorsal epilation..... 8d. 50% annular epilation.....17d.	100% annular epilation
	658	200	5.0	10% annular epilation..... 9d. 100% annular epilation with constriction.....17d.	100% annular epilation with constriction
	596	250	524	10% dorsal epilation..... 7d. 100% annular epilation.....15d.	Spontaneous amputation, 21d.
	659	250	5.0	5% dorsal epilation..... 7d. 100% annular epilation.....17d.	Spontaneous amputation, 20d.
93:1	478	175	481	10% dorsal epilation.....13d. 100% annular epilation...17–28d.	100% dor., 95% vent. epil.
	361	175	5.1	10% dorsal epilation..... 7d. 100% dor., 50% vent. epil....14d.	100% dor., 50% vent. epil.
91:1	482	50	481	10% dorsal epilation.....15d. 10% annular epilation.....22d.	100% dorsal epilation
	536	50	5.3	10% dorsal epilation.....10d. 50% annular epilation.....13d.	95% dorsal epilation
	481	75	481	10% dorsal epilation.....12d. 100% dor., 10% vent. epil....22d.	100% dorsal epilation
	535	75	5.3	10% dorsal epilation..... 9d. 100% dor., 50% vent. epil....13d.	100% dorsal epilation
	480	100	481	10% dorsal epilation.....12d. 100% annular epilation...15–22d.	100% dor., 10% vent. epil.
	534	100	5.3	10% dorsal epilation..... 8d. 100% annular epilation...13–15d.	100% dorsal epilation
88:1	479	150	481	10% dorsal epilation.....13d. 100% annular epilation...17–26d.	100% dor., 25% vent. epil.
	532	150	5.4	10% dorsal epilation..... 7d. 100% annular epilation...15–29d.	100% dor., 95% vent. epil.
	478	175	481	10% dorsal epilation.....13d. 100% annular epilation...17–28d.	100% dor., 95% vent. epil.
	531	175	5.5	10% dorsal epilation..... 7d. 100% annular epilation...15–24d.	100% dor., 25% vent. epil.

Table I (*Cont.*)

Ratios of Intensity	Animal No.	Dosage mc-min.	No. mc.	Tissue Reaction	
				Initial Reactions and Time of Appearance in Days	Final Reaction at 35th Day Post-Treatment
74:1	477	200	481	10% annular epilation..... 6d. 100% annular epilation with constriction.....13d.	100% annular epilation
	529	200	6.5	10% dorsal epilation.....11d. 100% annular epilation with constriction.....14d.	100% annular epilation with constriction
	476	250	481	100% annular epilation.....10d. constriction.....13d.	Spontaneous amputation, 19d.
	530	250	6.5	10% dorsal epilation..... 9d. 100% annular epilation with constriction.....14d.	Spontaneous amputation, 16d.
50:1	400	125	251	5% annular epilation..... 7d. 100% annular epilation..... 8d.	100% dor., 90% vent. epil.
	427	125	5.0	10% dorsal epilation..... 8d. 100% annular epilation.....12d.	95% annular epilation
42:1	403	175	251	10% dorsal epilation..... 7d. 100% annular epilation with constriction.....12d.	100% annular epilation with constriction
	424	175	6.0	10% annular epilation..... 8d. 100% annular epilation with constriction.....11d.	Spontaneous amputation, 25d.
39:1	167	150	193	10% annular epilation.....11d.	100% dor., 25% vent. epil.
	223	150	5.0	10% annular epilation.....12d.	100% dor., 25% vent. epil.
36:1	400	125	251	5% annular epilation..... 7d. 100% annular epilation..... 8d.	100% dor., 90% vent. epil.
	423	125	7.0	10% annular epilation..... 9d. 100% annular epilation.....11d.	95% dor., 80% vent. epil.
	402	200	251	5% dorsal epilation..... 7d. 100% annular epilation with constriction .....11d.	Spontaneous amputation, 27d.
	422	200	7.0	10% annular epilation..... 9d. 100% annular epilation with constriction .....11d.	Spontaneous amputation, 17d.
	401	250	251	10% dorsal epilation..... 6d. 100% annular epilation..... 8d.	Spontaneous amputation, 12d.
	419	250	7.0	10% dorsal epilation..... 5d. 100% annular epilation with constriction .....11d.	Spontaneous amputation, 16d.

TABLE I (*Cont.*)

Ratios of Intensity	Animal No.	Dosage mc-min.	No. mc.	Tissue Reaction	
				Initial Reactions and Time of Appearance in Days	Final Reaction at 35th Day Post-Treatment
31:1	545	150	154	10% dorsal epilation..... 8d. 100% annular epilation...13–19d.	100% dor., 80% vent. epil.
	574	150	5.0	10% dorsal epilation.....13d. 100% annular epilation.....21d.	100% annular epilation
28:1	499	100	146	10% dorsal epilation.....10d.	100% dorsal epilation
	534	100	5.3	10% dorsal epilation..... 8d. 50% dor., 10% vent. epil....10d.	100% dorsal epilation
26:1	496	200	171	10% dorsal epilation..... 9d. 100% annular epilation.....12d.	100% dor., 95% vent. epil.
	529	200	6.5	10% dorsal epilation.....11d. 100% annular epilation with constriction .....14d.	100% annular epilation with constriction
21:1	618	75	85	5% dorsal epilation.....11d. 100% dorsal epilation.....16d.	100% dorsal epilation
	665	75	4.0	10% dorsal epilation..... 8d. 50% annular epilation.....11d.	100% dor., 10% vent. epil.
	619	100	85	100% dorsal epilation.....11d. 10% ventral epilation.....23d.	100% dor., 10% vent. epil.
	663	100	4.0	10% dorsal epilation..... 9d. 50% dor., 10% vent. epil....11d.	100% dor., 10% vent. epil.
	620	125	85	10% dorsal epilation.....11d. 100% dor., 10% vent. epil....14d.	100% dor., 90% vent. epil.
	662	125	4.0	10% dorsal epilation..... 8d. 10% annular epilation.....12d.	100% dor., 90% vent. epil.
	598	150	524	10% dorsal epilation.....14d. 100% dor., 10% vent. epil....17d.	100% annular epilation
	628	150	25	10% annular epilation..... 7d.	100% dor., 80% vent. epil.
	597	200	524	10% dorsal epilation..... 8d.	100% annular epilation
	625	200	25	10% dorsal epilation..... 7d. constriction .....18d.	100% annular epilation
	596	250	524	10% dorsal epilation..... 7d. 100% annular epilation.....15d.	Spontaneous amputation, 21d.
	624	250	25	10% dorsal epilation..... 7d. 100% annular epilation with constriction .....16d.	Spontaneous amputation, 19d.

Table I (*Cont.*)

Ratios of Intensity	Animal No.	Dosage mc-min.	No. mc.	Tissue Reaction	
				Initial Reactions and Time of Appearance in Days	Final Reaction at 35th Day Post-Treatment
18:1	583	125	71	10% dorsal epilation.....10d.	100% annular epilation
	612	125	4.0	10% dorsal epilation..... 9d.	100% annular epilation
	582	250	71	10% dorsal epilation..... 7d.	Spontaneous amputation, 14d.
	608	250	4.0	10% dorsal epilation..... 5d.	Spontaneous amputation, 16d.
9:1	321	5	221	No apparent reaction	No apparent reaction
	337	5	23	No apparent reaction	No apparent reaction
	108	100	227	10% dorsal epilation.....10d. 10% annular epilation.....14d.	100% dorsal epilation
	131	100	26	10% dorsal epilation.....17d. 100% dor., 10% vent. epil....19d.	100% dorsal epilation

Summary of results from treatments with the unfiltered radon bulb. Data grouped according to ratios of intensity differences. Pairs of animals received the same number of millicurie-minutes with the same radon bulb but with varying degrees of radiation intensity.

shown in Tables II and III. In Table II are shown instances where there is apparently a slightly greater reaction resulting from the bulbs when used strong, and in Table III are four instances where the swing is apparently in the opposite direction. But the differences tend to cancel each other, and a close inspection of the entire course of the radiation history shows that the differences are actually very slight. Take for instance the first pair of animals in Table II. The final reaction for animal No. 598 was complete annular epilation over the treated area, and for No. 661, complete dorsal epilation with a very slight ventral epilation. Still, from the 19th to 25th day the latter animal had a fairly moderate ventral epilation.

For the second and fourth pairs of treatments the dosages were so low (15 and 25 millicurie-minutes respectively) that the differences in final reactions are very slight and it is difficult to make any statement as to the significance of the results.

2. *The gold-platinum tube* (4.25 *millimeters from the dorsal surface of the tail to the center of radiation*).

The results shown in Table IV are presented in a slightly different manner than in the previous tables. Radon tube No. 4 was obtained when showing a strength of 247 mc. It was then used to treat five mice, Nos. 829 to 833, all of the same age and from the same litter. A dose of 100 millicurie-hours was kept constant throughout the experiment. By the time the last mouse was ready for treatment the tube had decreased in strength to 239 mc. Table IV shows the animal number, the millicurie-hours, the number of millicuries and the tissue reactions. A few days later the same tube was used on a similar series of mice, with the dose remaining the same but the strength of the tube varying from 171 to 167 mc. Similarly five more mice were treated when the strength of the tube was about 80 mc.

It will be noted that the tissue reactions shown in Table IV, for mice Nos. 829 to 843 inclusive, are essentially similar. The

TABLE II

Ratios of Intensity	Animal No.	Dosage mc-min.	No. mc.	Tissue Reaction	
				Initial Reactions and Time of Appearance in Days	Final Reaction at 35th Day Post-Treatment
131:1	598	150	524	10% dorsal epilation.....14d. 100% annular epilation.....21d.	100% annular epilation
	661	150	4.0	10% dorsal epilation..... 8d. 100% dor., 50% vent. epil. 19–25d.	100% dor., 5% vent. epil.
43:1	320	15	221	5% dorsal epilation.....13d.	Complete return of hair
	362	15	5.1	No apparent reaction	No apparent reaction
21:1	598	150	524	10% dorsal epilation.....14d. 100% annular epilation.....21d.	100% annular epilation
	627	150	25	10% dorsal epilation..... 9d. 80% annular epilation.....16d.	100% dorsal epilation
9:1	319	25	221	10% dorsal epilation.....12d.	5% dorsal epilation
	341	25	23	No apparent reaction	No apparent reaction

Summary of results, a continuation of Table I, showing pairs of treatments wherein the dose delivered by the greater intensity gave a slightly greater tissue reaction.

first epilations appear between the 4th and 6th day after treatment and there is complete annular epilation from the 12th to the 22d day. Complete annular epilation is the final reaction except in two instances (Nos. 841 and 842) where the hair returned to a slight degree on the ventral surface.

Now in all these treatments the ratio of intensities is no greater than approximately 3:1, and the time of exposure varies from slightly less than thirty minutes to a little over sixty minutes.

In the final series of treatments with the same tube at still weaker strengths the treatment times increase from about five hours to twenty-five and even to slightly over fifty hours. *

In the last three treatments (Nos. 859, 881 and 887), the final reaction is somewhat less than that following the doses from the tube when strong. The intermediate reactions in these instances, however, show that the maximum tissue reaction was complete annular epilation on the 24th and 15th day in Nos. 859 and 881 respectively, and only slightly less than this reaction in No. 887. The significance of the difference in the final reactions as shown in these last three cases will be discussed later in this paper.

Table V gives the results from two series of treatments by gold-platinum tube No. 3. Here again it will be noted that as the strength of the tube decreased the final reactions showed a decreased effect. By looking at the intermediate reactions it will be seen that even following the treatments of longest duration (Nos. 713 and 700) the maximum tissue reactions were considerably higher than the final reaction. This merely means that there was a recovery effect from the treatments.

3. *The radon bulb, with 2 mm. of brass filtration and 4.25 mm. from the dorsal surface of the tail to the center of radiation.*

*The time of very long treatments is determined by the use of the formula mc-hr.$=133\ I_o\ (1-e^{-.0075T})$, in which I_o=initial strength of the source in mc.; e=the base of natural logarithm and T=time in hours (see Failla[3]).

In Table VI is a summary of the results from treatments with the radon bulb inclosed in a 2 mm. brass applicator and applied so that the center of the source of radiation was 4.25 mm. from the dorsal surface of the tail.

In the first three instances shown in the table there apparently is an irregularity in the final reactions. It will be well to note, however, that the severity of reaction in these cases must be judged by the peak of the tissue response. Nos. 687 and 704 both show complete annular epilation on the 16th day post-treatment. The recovery processes as shown by the return of hair, were slightly greater in No. 704 than in No. 687. In animal No. 712 the maximum epilation effect was a moderate annular epilation, or what we have designated as approximately 50 per cent annular epilation, occurring twenty-two days post-treatment. The recovery was not as complete on the 35th day, as that which occurred in Nos. 687 and 704.

In the last four treatments of Table VI there is again practically the same maximum tissue response in each instance. The final reaction for the dose following exposure to the bulb when of the weakest strength is less than the final reactions noted for the bulb when stronger.

DISCUSSION OF RESULTS

When the unfiltered radon bulb was used when strong and then when weak the actual time of exposure in each instance was relatively short. With the ratios of intensities at 541:1 (See Nos. 522 and 594) the actual

TABLE III

Ratios of Intensity	Animal No.	Dosage mc-min.	No. mc.	Tissue Reaction	
				Initial Reactions and Time of Appearance in Days	Final Reaction at 35th Day Post-Treatment
541:1	522	100	541	10% dorsal epilation.....12d. 100% dor., 10% vent. epil....18d.	100% dorsal epilation
	594	100	1.0	10% annular epilation.....11d. 100% dor., 90% vent. epil....16d.	100% dor., 60% vent. epil.
449:1	635	75	515	10% dorsal epilation.....19d. 100% dorsal epilation.....22d.	100% dorsal epilation
	701	75	1.2	10% dorsal epilation..... 9d. 100% annular epilation.....28d.	100% dor., 50% vent. epil.
63:1	169	150	157	10% dorsal epilation..... 7d. 100% annular epilation...11–22d.	100% dorsal epilation
	235	150	2.5	10% annular epilation.....11d. 100% annular epilation with constriction.....17d.	100% annular epilation with constriction
44:1	172	150	110	10% annular epilation..... 8d. 10% dor., 50% vent. epil....17d.	100% dorsal epilation
	235	150	2.5	10% annular epilation.....11d. 100% annular epilation with constriction.....17d.	100% annular epilation with constriction

Summary of results, a continuation of Tables I and II showing pairs of treatments wherein the dose delivered by the small intensity gave a greater tissue reaction.

Table IV

Animal No.	Dosage mc-hr.	No. mc.	Tissue Reaction	
			Initial Reactions and Time of Appearance in Days	Final Reaction at 35th Day Post-Treatment
829	100	247	10% annular epilation..... 4d. 100% annular epilation.....14d.	100% annular epilation
830	100	246	10% annular epilation..... 4d. 100% annular epilation.....12d.	100% annular epilation
831	100	245	20% dor., 10% vent. epil..... 4d. 100% annular epilation.....17d.	100% annular epilation
832	100	244	10% annular epilation..... 4d. 100% annular epilation.....12d.	100% annular epilation
833	100	239	10% annular epilation..... 4d. 100% annular epilation.....19d.	100% annular epilation
834	100	171	10% annular epilation..... 4d. 100% annular epilation.....20d.	100% annular epilation
835	100	170	5% annular epilation..... 4d. 100% annular epilation.....20d.	100% annular epilation
836	100	169	10% annular epilation..... 4d. 100% annular epilation.....22d.	100% annular epilation
837	100	168	10% annular epilation..... 4d. 100% annular epilation.....20d.	100% annular epilation with constriction
838	100	167	10% annular epilation..... 4d. 100% annular epilation.....17d.	100% annular epilation
839	100	83	10% annular epilation..... 6d. 100% annular epilation.....16d.	100% annular epilation
840	100	82	5% dorsal epilation..... 6d. 100% annular epilation.....16d.	100% annular epilation with constriction
841	100	81	5% annular epilation..... 6d. 100% annular epilation.....15d.	100% dor., 95% vent. epil.
842	100	81	10% annular epilation..... 6d. 100% annular epilation.....21d.	100% dor., 85% vent. epil.
843	100	80	5% annular epilation..... 6d. 100% annular epilation.....16d.	100% annular epilation
857	100	23	5% ventral epilation..... 6d. 100% annular epilation.....16d.	100% dor., 90% vent. epil.
858	100	22	5% annular epilation..... 6d. 100% annular epilation.....14d.	100% dor., 50% vent. epil.
859	100	13	10% dorsal epilation..... 7d. 100% annular epilation.....24d.	90% dor. epil., with 50% vent epil. over small area

Table IV (*Cont.*)

Animal No.	Dosage mc-hr.	No. mc.	Tissue Reaction	
			Initial Reactions and Time of Appearance in Days	Final Reaction at 35th Day Post-Treatment
881	100	4	10% dorsal epilation..... 7d. 100% annular epilation.....15d.	90% dor. epil., with 90% vent. epil. over very small area
887	100	2	5% annular epilation.....12d. 90% dor., 100% vent. epil.....24d.	95% dor., 5% vent. epil.

Summary of results from treatments with gold-platinum tube No. 4. Each treatment was for 100 mc-hr. and the data are arranged according to the order of the intensity of the radon.

time of treatment was eleven seconds in one instance and 100 minutes in the other. In the majority of experiments the longest beta-ray treatments, with the exception of No. 702 (182 minutes), were rarely over 100 minutes. We know that an untreated tail of a mouse, of the age used in the experiments, grows about 2.5 mm. in length in twenty-four hours. The actual growth span during the longest beta-ray treatments was therefore small. We also know that the confinement of the animal for relatively short intervals when no radiation is given does not appreciably reduce the subsequent rate of growth of the tail. However, when gamma-ray radiation is used the time factor alone

Table V

Animal No.	Dosage mc-hr.	No. mc.	Tissue Reaction	
			Initial Reactions and Time of Appearance in Days	Final Reaction at 35th Day Post-Treatment
681	100	226	10% dorsal epilation.....10d. 100% annular epilation.....22d.	100% annular epilation
690	100	74	10% dorsal epilation..... 9d. 100% dor., 10% vent. epil.....28d.	100% dor., 80% vent. epil.
699	100	21	10% dorsal epilation.....15d. 80% dor., 5% vent. epil.....18d.	80% dor., 5% vent. epil.
713	100	5	50% dor., 10% vent. epil.....12d. 80% dor., 50% vent. epil.....28d.	10% dorsal epilation
682	70	225	10% dorsal epilation.....13d. 50% annular epilation.....20d.	50% dorsal epilation
683	70	187	5% annular epilation.....12d. 50% annular epilation.....19d.	50% dor., 5% vent. epil.
691	70	73	10% annular epilation.....14d. 50% annular epilation.....22d.	50% dorsal epilation
700	70	20	10% dorsal epilation.....16d. 50% dor., 5% vent. epil.....18d.	5% dorsal epilation

Summary of results from treatments with gold-platinum tube No. 3. Data show tissue reactions for 100 and 70 mc-hr. respectively, arranged according to order of intensity of radon.

appears to inject an important element for consideration. The majority of the treatments with filtered radiation were given during intervals of less than five hours. We have found from a study of control animals that confinement on the irradiation apparatus without exposure to radiation for intervals of one to five hours, does not appreciably retard the subsequent growth of the tail. When the young animals are kept from feeding and confined for twenty-four hours we find no appreciable growth of the tail during that period. For ninety-two hours of confinement it was necessary to remove the animals for one hour each day and permit of fifty minutes of nursing. The tails of these animals remained virtually stationary in length, showing in each case but a millimeter of growth for the entire four days.

With the above facts in mind we see that gamma-ray treatments for over twenty-four hours act upon a tail that is growing less rapidly towards the end of the exposure than it was at the beginning of exposure. This brings in the factor of rate of growth in relation to subsequent radiation changes. If we agree that tissues whose rate of growth or differentiation is depressed show a less vigorous response to radiation than do more rapidly growing tissues, then that factor will have to be taken into consideration in the results recorded in this paper. In other words, the long gamma-ray treatments (using a weak source of radiation) resulted in a slightly decreased tissue reaction as compared with the same dose delivered over a shorter period, but this change may be due not only to the factor of intensity difference in the source of radiation, but to the factor of decreased rate of growth of the treated tissues towards the end of the exposure. The rate of growth in this instance may be due to the experimen-

TABLE VI

Animal No.	Dosage mc-hr.	No. mc.	Tissue Reaction	
			Initial Reactions and Time of Appearance in Days	Final Reaction at 35th Day Post-Treatment
687	125	361	10% dorsal epilation.....10d. 100% annular epilation.....16d.	25% dor., 5% vent. epil.
704	125	43	10% annular epilation..... 8d. 100% annular epilation.....16d.	5% dorsal epilation
712	125	17	5% dorsal epilation..... 8d. 50% annular epilation.....22d.	50% dor., 10% vent. epil.
732	160	432	10% annular epilation.....10d. 100% annular epilation.....19d.	100% annular epilation
737	160	151	10% annular epilation..... 5d. 100% annular epilation.....14d.	100% annular epilation
747	160	51	10% dorsal epilation..... 7d. 90% annular epilation.....26d.	90% annular epilation
777	160	11	50% annular epilation..... 8d. 95% annular epilation.....22d.	50% dorsal epilation

Summary of results from treatments with radon bulb in an applicator with 2 millimeters of brass filtration. Data show tissue reactions for 125 and 160 mc-hr. respectively, arranged according to order of intensity of radon. The first three treatments were given by bulb No. 1 and the remainder by bulb No. 2.

tal methods alone (fasting, etc.) and not to the action of the radiation.

CONCLUSIONS

1. On the whole, our experiments tend to show that the Bunsen-Roscoe Law is applicable within the limits investigated for the beta-ray treatments of the tissues we used.

2. With the gamma-ray exposures the same condition holds over the upper range of treatments, but not for the treatments with a source of radiation which is very weak. In these instances the lesser effect was obtained when the applicator of weaker strength was used. This reaction may be due not only to intensity differences alone, but indirectly to an arrest in the growth of the tissues being irradiated as a result of the experimental procedures incident to the prolonged restraint of the animal during the longer exposures.

3. From a practical point of view it is interesting to note that our results would indicate that in treating superficial lesions of the skin with unfiltered radon, the operator may expect to obtain similar clinical results from using sources of radiation which may vary over a fairly wide range of intensities.

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DISCUSSION

Dr. Douglas P. Murphy, Philadelphia. Drs. Bagg and Halter, in carrying out their present experiments, have probably led us to the settlement of one of the most important problems concerned with the therapeutic use of radium; they have answered a question which has been the subject of much discussion since the earliest use of radium therapy.

We now realize that small amounts of radium are as efficient as larger ones, provided an adequate length of exposure is given to the tissue under treatment. Knowledge of this fact is of great value to the clinician. Though he may have at hand only a small amount of radium, he will feel reassured that when properly applied, it will be as efficient in its action as a much larger amount applied for a much shorter period of time. Such knowledge will in all probability lead to a greater use of radium, since small amounts of the element are always more easily secured than the larger ones.

This principle being true with respect to the use of radium, in all probability it also holds with respect to the use of the roentgen ray, when contrasting the relative efficiency of the low milliamperage of the air-cooled tubes and the higher power of the water-cooled tubes. It will stimulate the possessors of tubes requiring longer periods of exposure, to further interest in their efforts with this form of apparatus.

The observations of Drs. Bagg and Halter, therefore, not only have led to a satisfying of our curiosity regarding the problem which they have investigated, but at the same time have cleared the way for an increased use of both radium and the roentgen ray in the field of human therapy.

Dr. H. J. Ullmann, Santa Barbara, Calif. I understood Dr. Murphy to say something that I think should not go in the records without discussion. I understood him to say that Dr. Bagg's paper would lead us to think we could treat cancer with small amounts of radium. As there are still some men treating carcinoma of the cervix with small amounts of radium, I feel that we should go on record as a society of not approving any inadequate treatment of cancer, and one cannot treat cancer, particularly of the cervix, with small quantities of radium.

THE DIVERGENCES BETWEEN ANTICIPATED AND OBSERVED RESULTS OF IRRADIATION OF PATHOLOGICAL TISSUES*

By FRED W. STEWART, M.D.*
Memorial Hospital
NEW YORK CITY

CONCLUSIONS drawn from studies of the effects of irradiation on normal tissues are of but limited value in estimating the effects to be realized on pathological tissues. The reason for this is quite apparent. A normal tissue or organ is a relatively standardized structure with a definite morphology and a metabolism at least fixed within physiological limits. Pathological tissues—and by this in the discussion we refer to the neoplastic diseases—exhibit wide differences in structure, metabolism, physiology and in their relations to their local environment and the body as a whole.

Essentially nothing is known concerning the relation of tumor metabolism and physiology to radiosensitivity. Practically all we know concerns the relation of structure and local environment to radiosensitivity. That radiosensitivity bears some relation to physiology seems probable from certain tumors, notably those of the ovary, the uterine myomas, perhaps thyroid carcinoma, possibly breast cancer and from the results observed in irradiating tumors in cachectics. The balance of the neoplastic group of diseases constitutes a virgin field for the investigator in this direction.

When we come to the question of structure and radiosensitivity we have many laws—some simple, others complex. It is easy to lay down laws when one has but small experience to test their validity. In tumor radiosensitivity almost every generalization must be qualified. In the first place, there is no definition of the term "radiosensitive." Does it mean that the tumor regresses completely? Does it mean that it fails to recur locally? Does it mean partial regression? Should time factors enter into the definition to distinguish the type of regression seen, for example, in lymphosarcoma, from that in a few slowly growing neurogenic sarcomas which take months or even years to disappear? Then, what tumor dose is meant? Until we speak the same language we can scarcely approach the question of radiosensitivity with any degree of accuracy.

Radiosensitivity is said to depend upon the embryonal quality of a tumor, the degree of anaplasia, the fundamental tissue of origin, the degree of papillary character, the cellularity, the circulatory status of the tumor, the nature of the tumor bed, the presence or absence of infection, the general status of the individual (anemia, cachexia, etc.). These factors are well known but do not permit too great generalizations. Furthermore they constitute a heterogeneous group—primitive type features, cellular constitution and organoid make-up, location and bed, infection, bodily status. All these factors are interrelated, often difficult to ascertain in their completeness and yet no reasonably accurate radiosensitivity determination is possible without knowing all of them. Is it then remarkable that oncologists of wide experience make many errors? The oncologist who wishes to perfect himself in this direction must be in close touch with a large clinic where accurate observations are made on tumor responses to known tumor doses. It will surely require years of accurate combined clinical-pathological observations to bring the radiosensitivity question to a point of true accuracy and the present situation in many clinics of the isolated pathologist, the often but slightly interested clinician, and the absent

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physicist is scarcely apt to improve knowledge in this direction. At the Memorial Hospital we have no illusions that we possess the necessary data on radiosensitivity but certain departments are making earnest efforts to acquire them.

We can definitely state that every law of radiosensitivity so far promulgated as a generalization is subject to exception, and the remainder of this paper is best devoted to examples of exceptions—some analyzable, others not as yet. One might select embryonal quality as a beginning. Embryonal testicular tumors, as a rule, show decreasing radiosensitivity in the following order: (1) diffuse embryonal carcinoma with lymphoid stroma; (2) embryonal adenocarcinoma (adenoma malignum); (3) relatively adult-looking tumors—for example, squamous cancers, in complex teratoma. A given tumor, let us say an embryonal carcinoma with lymphoid stroma, undergoes complete necrosis with a dosage "X," a second tumor of the same sort behaves differently, obviously because the local factors are complex. One of the local factors I believe we have analyzed in a few cases and that is the relation of the tumor to the tunica albuginea. The latter is a tense fibrous capsule. When the tumor has filled the testis and has perforated this tunic there will be found a dosage "X" which will have destroyed the tumor *within* the tunic but not *without*. This destruction appears therefore to be not only a direct radiation effect on the cell but on the cell in relation to restraining factors, the tense tunica, and the result is due to the irradiation of the tumor cell plus radiation edema. Since the latter occurs in a tight, moderately elastic capsule the tumor cells are killed not only by radiation but also by pressure and resultant circulatory anemia. The dosage "X" is therefore not a destructive dose for embryonal carcinoma with lymphoid stroma but for this tumor under certain existent conditions. With invasion of the tunic and the aquisition of a blood supply independent of mechanical factors, the killing dose is higher.

The nature of the fundamental tissue of origin is important for the radiosensitivity of a tumor but this relationship is unexplained. Moreover there appears to be no general relation between the susceptibility of the normal tissue to irradiation and the radiosensitivity of tumors derived from such tissue. We find agreements and discrepancies. Three such examples may be selected, first the neurogenic sarcomas. These are common sarcomatous tumors comprising the bulk of the soft part sarcomas. They are of neural origin since they arise from Schwann cells. Nerve tissue is very radioresistant and it is therefore not remarkable that these neurogenic tumors as a group are among the most radioresistant. This likewise holds true for the gliomas and the melanomas. The tumors are so resistant that extreme cellularity or anaplasia adds little to their observed sensitivity. These tumors may be taken to illustrate resistant tumors arising in resistant soil. Secondly, the liposarcomas. These tumors in our experience are apt to be radiosensitive often to a marked degree. When anaplastic they may melt down like lymphosarcoma. Even when they contain well-developed tumor fat cells they may still be quite sensitive. Yet fat tissue and simple lipomas are resistant structures. Fat tissue itself breaks down into oil cysts, fatty and crystalline detritus and there occurs an indolent chronic inflammatory lesion. Thus in contradistinction to the neural group, we have a sensitive tumor arising from a resistant soil. Thus the most necessary thing to know about these soft part sarcomas to predict their radiation behavior is the fundamental tissue of origin, i.e., lipogenic or neurogenic, although just why this is the case is at present beyond our knowledge. A third example lies in the lymphosarcomas. We know that normal lymph nodes are rather resistant structures, that they withstand the irradiation necessary to destroy many metastatic carcinomas. One incidental observation has enabled us to say that a node which has received nearly 5 S.E.D. at least retained or so reëstablished

its integrity that it served within a few months as a filtering-out mechanism for metastatic epidermoid carcinoma. On the other hand, lymphosarcomas form one of the most radiosensitive groups of neoplasms and may occasionally regress markedly under doses which are scarcely more than fluoroscopic quantities—almost like a catalytic action. The entire situation suggests the presence of some entirely unknown factor or factors influencing the sensitivity of the tumor process.

Papillary tumors tend in general to be more sensitive than non-papillary tumors but the mere fact that a tumor is papillary does not mean that it is sensitive. In epidermoid carcinomas of the intraoral cavity or the cervix my experience has been that the type of circulation largely determines the primary regression. Tumors with a delicate capillary supply are usually sensitive. These tumors are usually soft, pinkish and granular looking. Many occur in the anterior floor of the mouth adjacent to the frenum. In the cervix the papillary growths over the vaginal portion of the cervix may melt under external radiation alone, whereas the same tumor extending up the cervical canal where its structure will be infiltrative will remain essentially unaltered. The hard, squamous, warty, carcinomas with well-developed thick-walled vessels are almost uniformly radioresistant. Occasional rare exceptions may be encountered at the base of the tongue. Papillary adenocarcinomas growing within cysts of the breast are moderately sensitive. Papillary adenoma malignum of the rectum is almost uniformly resistant and whereas there is reason to believe that papillary carcinomas of the bladder should be sensitive the doses so far applied to the bladder are too large to render judgment as to sensitivity possible. Thus when we analyze the influence of papillary character on sensitivity to irradiation, we step immediately into two other fields—location and character of blood supply.

Increasing cellularity often means increasing sensitivity but other factors enter in. Neurogenic sarcomas, gliomas, melanomas, seem radioresistant despite their cellularity and, if they are definitely more sensitive, the more cellular and anaplastic they appear under the microscope, then this increased sensitivity is too slight to be perceptible with any degree of uniformity under the doses suitable for treatment. The relation between cellularity and response to irradiation—all other factors being equal—must be separately determined in the different neoplastic groups. Blanket rules lead nowhere.

Tumor sensitivity differs according to tumor bed. A tumor reacting well in its primary location may react poorly in its bony metastases, but, on the other hand, other features obscure the exact significance of this feature. Squamous carcinoma of the intraoral cavity invading bone is always accompanied by osteomyelitis which may have much to do with its resistance since infection always adversely influences radiosensitivity. The same is true of basal cell carcinoma. On the other hand, very frequently patients with the bone metastases of breast cancer experience marked relief from pain and the bones undergo recalcification and repair under doses usually insufficient to greatly affect the primary tumor. This is in rather marked contradistinction to what is usually seen in prostatic bone metastases. It would therefore appear that this question of influence of tumor bed requires separate analysis in different cases.

After all, the only law of radiosensitivity which remains essentially unchallenged is that one accomplishes very little by irradiating a cachectic patient unless the cachexia results from a highly sensitive tumor of the type of lymphosarcoma, thymoma, Wilms's tumor and the like.

The purpose of this paper is not an attempt to break down general laws which have a certain degree of wide applicability but to draw attention to the manner in which experience calls for constant modification of these general laws to fit the particular neoplasm in the particular individual. It serves likewise to show how little

studies of the effect of irradiation on normal tissues are translatable into the pathologic field. Attempts to correlate effects of irradiation of normal tissues with effects in the neoplastic field are fraught with much danger and are comparable in general only with attempts to conclude that because a chemotherapeutic agent is of value in one infectious disease affecting a given tissue or organ it is equally valuable in another. Studies of irradiation of normal tissues have produced interesting and important data. The bearing of such data on the treatment of neoplastic diseases has been considerable in connection with measurements of types of radiation, time factors and the like. Such work must be continued but its application to clinical procedure must be determined anew with each particular modification, bearing in mind the whole complex character of the neoplastic process.

DISCUSSION

Dr. Douglas Quick, New York City. Dr. Stewart has sounded a very important note of warning relative to the appraisal of expected reactions to irradiation based on histological differentiation. The pathologist is entitled to complete clinical data along with every specimen submitted in the same way that the clinician employs all clinical information relative to the case before offering an opinion from his standpoint. Dr. Stewart has emphasized a great many of the particular factors having a bearing on the ultimate histological prognostication. The variables are many but unless they are all thoroughly set down for the guidance of the pathologist, it is impossible to expect adequate expression of reasonable opinion as to the probable radiosensitivity from him. I think that emphasis of this point by Dr. Stewart now is very timely. We need to have the close cooperation of the pathologist not only from the laboratory angle but from the clinical side as well. We need also to have the cooperation of the pathologist in the beginning of the treatment period rather than after an avoidable error has been made through lack of sufficient conference in that direction.

THE GROUPING OF RADIUM TUBES IN PACKS OR PLAQUES TO PRODUCE THE DESIRED DISTRIBUTION OF RADIATION*

By EDITH H. QUIMBY, M.A.
Biophysics Department, Memorial Hospital
NEW YORK CITY

ONE of the conditions aimed at in external irradiation with packs or plaques is that the radiation shall be delivered as uniformly as possible over the area under the applicator. Evidently a uniformly irradiating surface will fulfill this condition only for very short distances from the skin, where each point receives by far the greatest part of its radiation from the portion of the applicator immediately above it. As the distance becomes appreciable, the radiation will be more intense

FIG. 1. Radium tube as subdivided into seven sources.

under the center than under the edges, due to the cross-fire from the various parts of the applicator. Given a continuous surface emitting unfiltered radiation, it should be possible to determine mathematically the required distribution of the radioactive material to produce a uniform distribution of radiation over a given area. However, in practice, the source is generally not continuous, but consists of an assortment of tubes or needles held in some sort of container, whence, obviously, the radiation is always filtered. The problem then becomes that of arranging these tubes or needles in their container to deliver the most nearly uniform radiation.

In order to decide how to do this, it is first necessary to know the distribution of radiation around any given tube or needle. This cannot be found accurately with any measuring instrument at present in use; for short distances or small tubes the size of the ionization chamber is always too large in comparison. It therefore becomes necessary to calculate these data. A number of papers have been published, by various authors, containing data of this sort for very limited ranges of length of tube, and of distance.[1–6] For the general problem it is necessary to have a much larger mass of information than is afforded by any of these. Accordingly calculations have been made for tubes from 1 to 6 centimeters long, each with a filter of 0.5 mm. gold,† in the following manner: Each tube was supposed to consist of seven sources distributed as shown in Figure 1. This, of course, is not strictly accurate, but with a larger number of sub-sources the mathematical labor involved increases rapidly, and this division gives a good approximation to the actual condition. At any given point outside the tube, the radiation delivered by the entire tube can be calculated as the sum of radiations from these seven sources, each considered for its own distance from the point in question, and due allowance being made for the change in filtration according to the angle at which the rays from that source traverse the tube.

Calculations of this sort were made for tubes of five different lengths, for a large number of points in different relative positions and at different distances from the tube, as shown in Figure 2. That is, for each tube, the relative intensities at 77 points were determined. From these data, the relative intensity of radiation delivered at any point by any tube, within the limits of the calculations, can be obtained. The entire data are given in Table 1, where the

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† This filter transmits only gamma radiation. Lighter filters are seldom used for external application, and the results for heavier ones would not be very different from these.

points A, B, C, etc., are successively 0.5 cm. farther out from the perpendicular to the center of the tube, as in Figure 2, and the distances are measured perpendicular to it. The values are in arbitrary units, based on an assumed value of 100 for a point source, having the same strength and filter as the tube, at a distance of 1 cm. They therefore mean nothing in themselves, but the ratios between them give the desired information. For example, with a tube 2 cm. long at a distance of 1 cm. from the skin, the intensity under its center (at A), is represented by 81 units, that under its end (at C) by 52.4 units, or 65 per cent as much, while that 1 cm. beyond the end of the tube (at E) is 20.2 units, or 25 per cent of that directly under the center.*

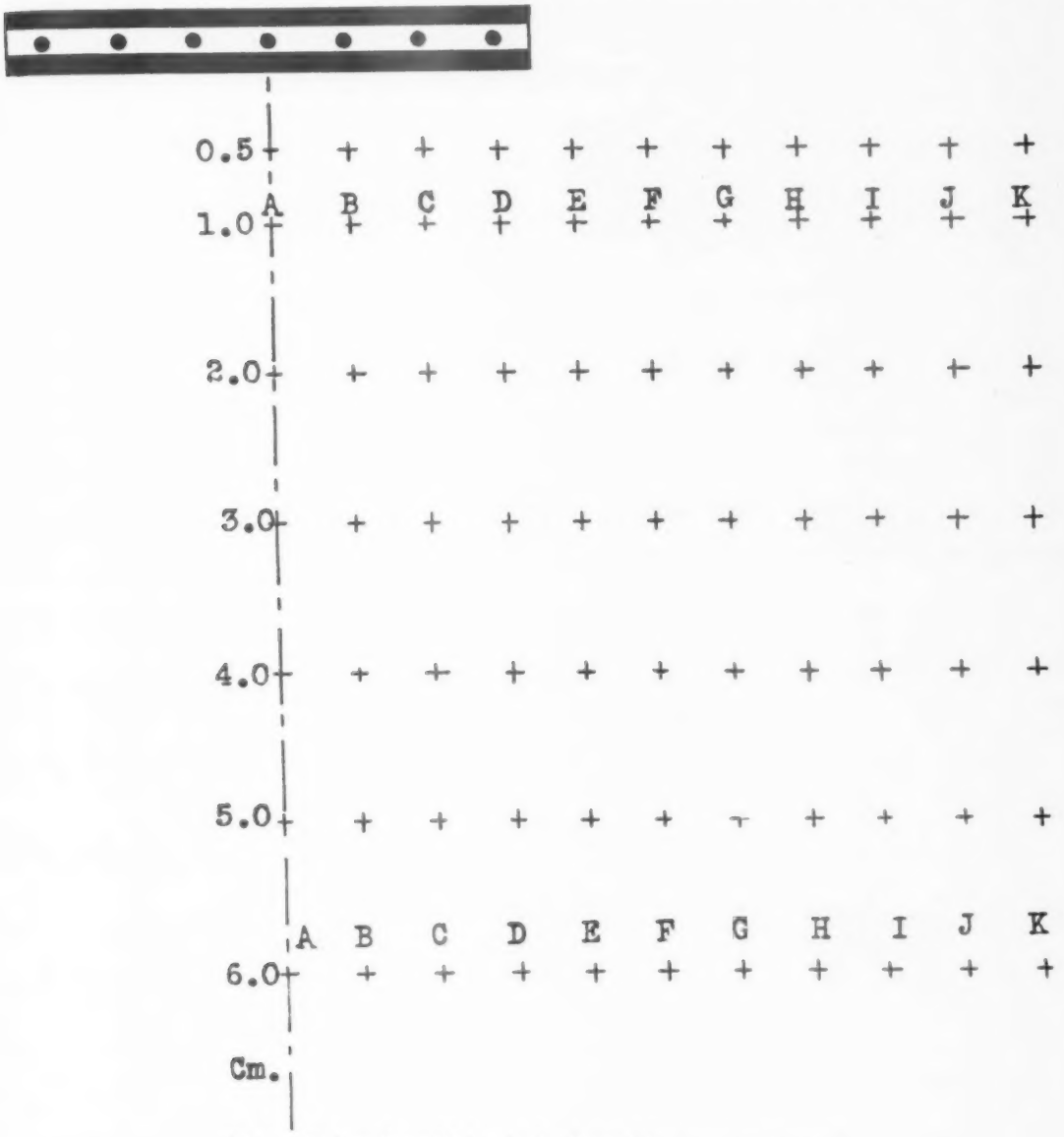


FIG. 2. Points for which relative intensities were computed.

* It would be possible to present all these data in terms of the erythema dose by specifying the strength of the tube and the duration of irradiation. This, however, would introduce complications into the practical applications of the table. The determination of actual doses from these data is simple, and will be dealt with later in the paper.

TABLE I

DISTRIBUTION OF RADIATION INTENSITY AROUND TUBES OF DIFFERENT LENGTHS BUT SAME RADIUM CONTENT. INTENSITY FROM POINT SOURCE AT 1 CM. ARBITRARILY TAKEN AS 100 UNITS

Point (Position with regard to Tube)*	Intensity from Point Source	Intensity from Tubes				
		1 cm. long	2 cm. long	3 cm. long	4 cm. long	5 cm. long
			0.5 cm. from source			
A	400.0	322.4	232.6	181.5	131.0	108.4
B	187.2	208.8	206.8	160.0	129.0	88.8
C	70.8	80.7	113.5	139.8	128.4	87.5
D	33.5	36.80	46.65	78.4	110.4	86.5
E	19.4	20.38	23.50	37.55	61.2	83.5
F	12.08	12.58	13.84	17.42	26.48	72.5
G	8.05	8.37	9.06	10.58	14.08	41.0
H	5.85	5.88	4.60	7.02	8.68	20.08
I	4.40		3.46	4.95	5.75	10.30
J	3.26		2.62	3.59		
K	2.53			2.71		
L	1.97			2.07		
			1.0 cm. from source			
A	100.0	93.5	81.0	68.6	52.8	39.8
B	79.0	77.2	73.0	63.1	52.6	39.6
C	46.9	48.8	52.4	53.8	50.6	39.3
D	26.8	29.20	32.48	38.58	37.76	39.0
E	17.93	18.41	20.15	24.24	30.64	35.3
F	12.10	12.30	13.24	15.92	19.58	29.9
G	8.42	8.70	9.00	10.35	12.88	21.4
H	6.23	6.43	6.65	7.35	8.53	13.8
I	4.76		5.08	5.99	5.55	9.3
J	3.81		3.92	4.21		
K	3.04		3.14	3.31		
L	2.42			2.66		
			2.0 cm. from source			
A	25.00	24.44	23.41	21.75	19.28	15.82
B	24.25	23.00	22.24	20.75	18.90	15.75
C	19.50	19.47	19.30	18.80	17.81	15.35
D	15.30	15.44	15.62	15.84	15.82	14.75
E	12.80	11.85	12.22	12.71	13.31	13.43
F	9.04	9.13	9.40	9.92	10.70	11.80
G	7.04	7.08	7.34	7.76	8.43	9.89
H	5.72	5.58	5.77	6.07	6.57	7.95
I	4.47		4.63	4.82	5.21	6.30
J	3.59		3.75	3.90		
K	3.00		3.09	3.20		
L	2.48			2.66		
			3.0 cm. from source			
A	11.11	11.04	10.76	10.36	9.70	8.58
B	10.73	10.70	10.50	10.12	9.55	8.45
C	9.85	9.82	9.70	9.38	9.11	8.28
D	8.65	8.67	8.63	8.57	8.40	7.92
E	7.40	7.44	7.46	7.50	7.52	7.35

TABLE I (*Cont.*)

DISTRIBUTION OF RADIATION INTENSITY AROUND TUBES OF DIFFERENT LENGTHS BUT SAME RADIUM CONTENT. INTENSITY FROM POINT SOURCE AT 1 CM. ARBITRARILY TAKEN AS 100 UNITS

Point (Position with regard to Tube)*	Intensity from Point Source	Intensity from Tubes				
		1 cm. long	2 cm. long	3 cm. long	4 cm. long	5 cm. long
			3.0 cm. from source			
F	6.26	6.30	6.33	6.43	6.55	6.62
G	5.24	5.27	5.32	5.45	5.62	5.92
H	4.40	4.41	4.46	4.59	4.78	5.14
I	3.70		3.78	3.86	3.94	4.40
J	3.22		3.22	3.27		
K	2.71		2.76	2.69		
L	2.41			2.38		
			4.0 cm. from source			
A	6.25	6.23	6.15	6.00	5.77	5.30
B	6.15	6.12	6.05	5.90	5.70	5.28
C	5.83	5.71	5.77	5.72	5.52	5.08
D	5.42	5.37	5.35	5.30	5.20	4.94
E	4.87	4.88	4.86	4.85	4.81	4.67
F	4.36	4.35	4.36	4.36	4.37	4.37
G	3.84	3.86	3.85	3.88	3.91	3.97
H	3.37	3.38	3.38	3.44	3.47	3.73
I	2.93		2.97	3.02	3.06	3.20
J	2.56		2.58	2.35		
K	2.27		2.28	2.05		
			5.0 cm. from source			
A	4.00	4.00	3.96	3.87	3.80	3.57
B	3.97	3.97	3.92	3.85	3.76	3.55
C	3.84	3.84	3.79	3.75	3.67	3.46
D	3.67	3.67	3.61	3.57	3.51	3.34
E	3.46	3.46	3.38	3.36	3.32	3.22
F	3.20	3.20	3.13	3.08	3.10	3.05
G	2.94	2.94	2.86	2.82	2.86	2.84
H	2.68	2.68	2.60	2.60	2.62	2.63
I	2.44		2.34	2.36	2.37	2.39
J	2.21		2.11	2.11		
K	2.00		1.90	1.90		
			6.0 cm. from source			
A	2.93	2.93	2.78	2.66	2.60	2.40
B	2.91	2.91	2.75	2.64	2.54	2.35
C	2.85	2.85	2.69	2.58	2.50	2.30
D	2.76	2.76	2.59	2.50	2.45	2.26
E	2.64	2.64	2.46	2.41	2.37	2.18
F	2.48	2.48	2.32	2.28	2.25	2.15
G	2.34	2.34	2.17	2.15	2.13	2.10
H	2.20	2.20	2.01	2.00	1.98	1.96
I	2.03		1.85	1.85	1.84	1.86
J	1.88		1.72	1.72	1.71	
K	1.77		1.57	1.57	1.57	

* For positions of these points relative to the tube, see Figure 4.

For any particular type of tube, the data may be used to the best advantage by plotting curves for the variation of intensity along lines perpendicular to the tube,—that is, all values for point A, at various distances, on one curve. Then data for distances not in the table can be read directly from the curves. Such curves, for a tube 2 cm. long, are given in Figure 3. Because of the wide range in values of the radiation

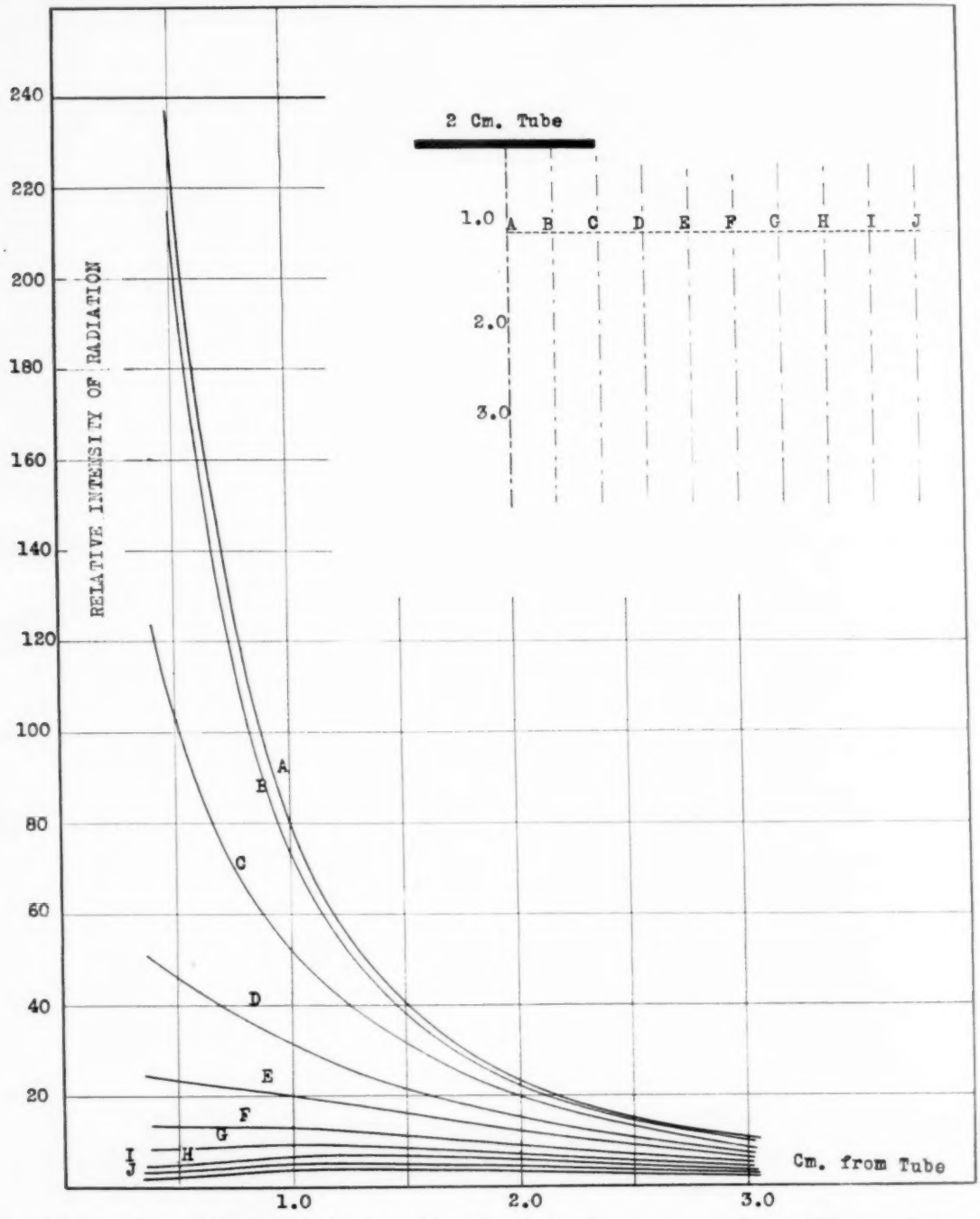


FIG. 3A. Curves showing relative intensities of radiation from a 2 cm. tube at different points.

with variation in distance, it is necessary either to use logarithms in plotting these data, or to make sets of curves for different parts of the range. The latter method has been chosen here to avoid the necessity of the extensive use of logarithm tables in subsequent calculations. From these curves the lines of equal intensity (isodose) around the tube can readily be determined. Such curves are given in Figure 4, for the 2 cm.

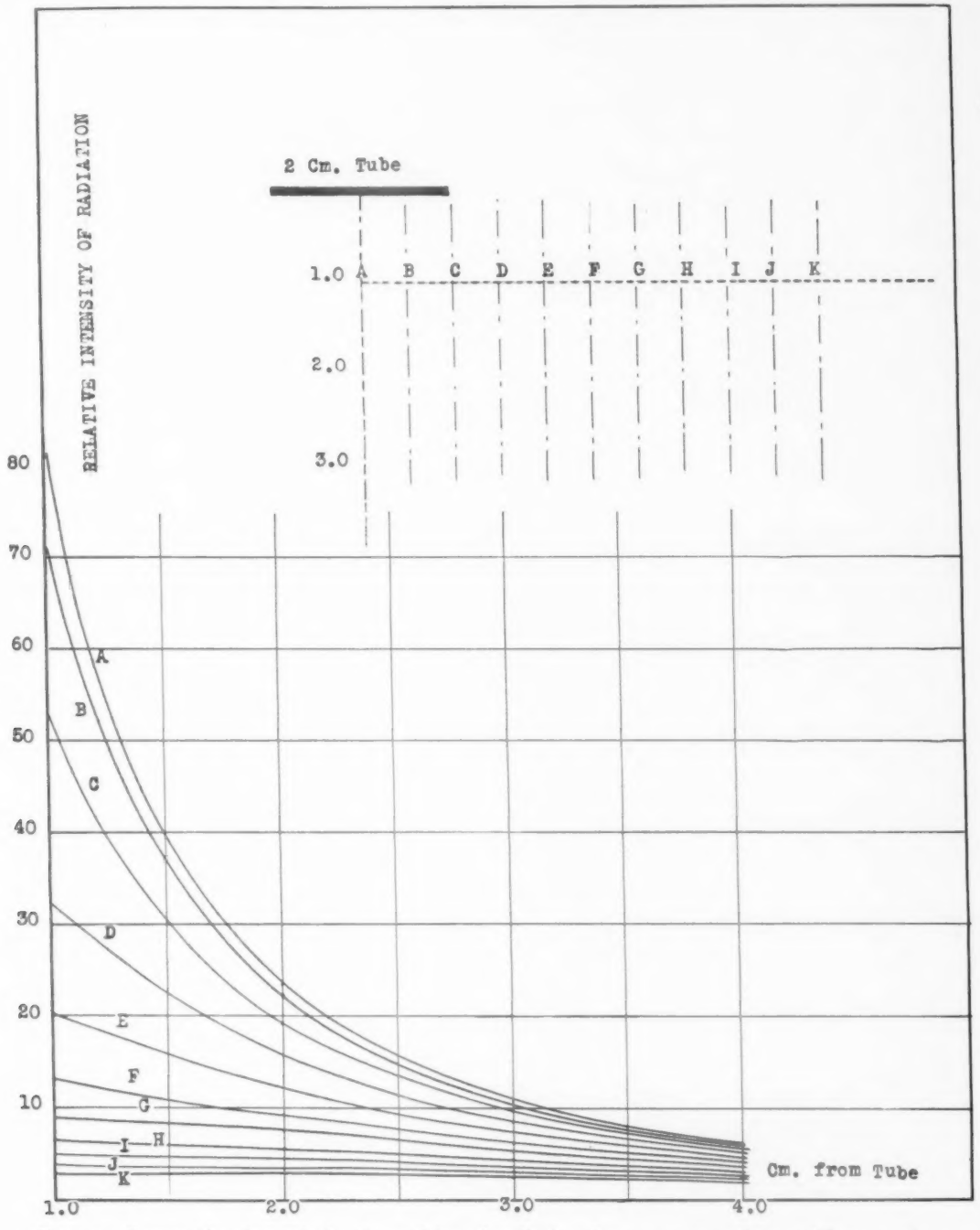


Fig. 3B. Curves showing relative intensities of radiation from a 2 cm. tube at different points.

tube as obtained from the curves of Figure 3, and for the 4 cm. one from similar curves not published.

as the following is carried out for every tube of the applicator. Figure 5 represents a 2 cm. tube at a distance of 3 cm. from the

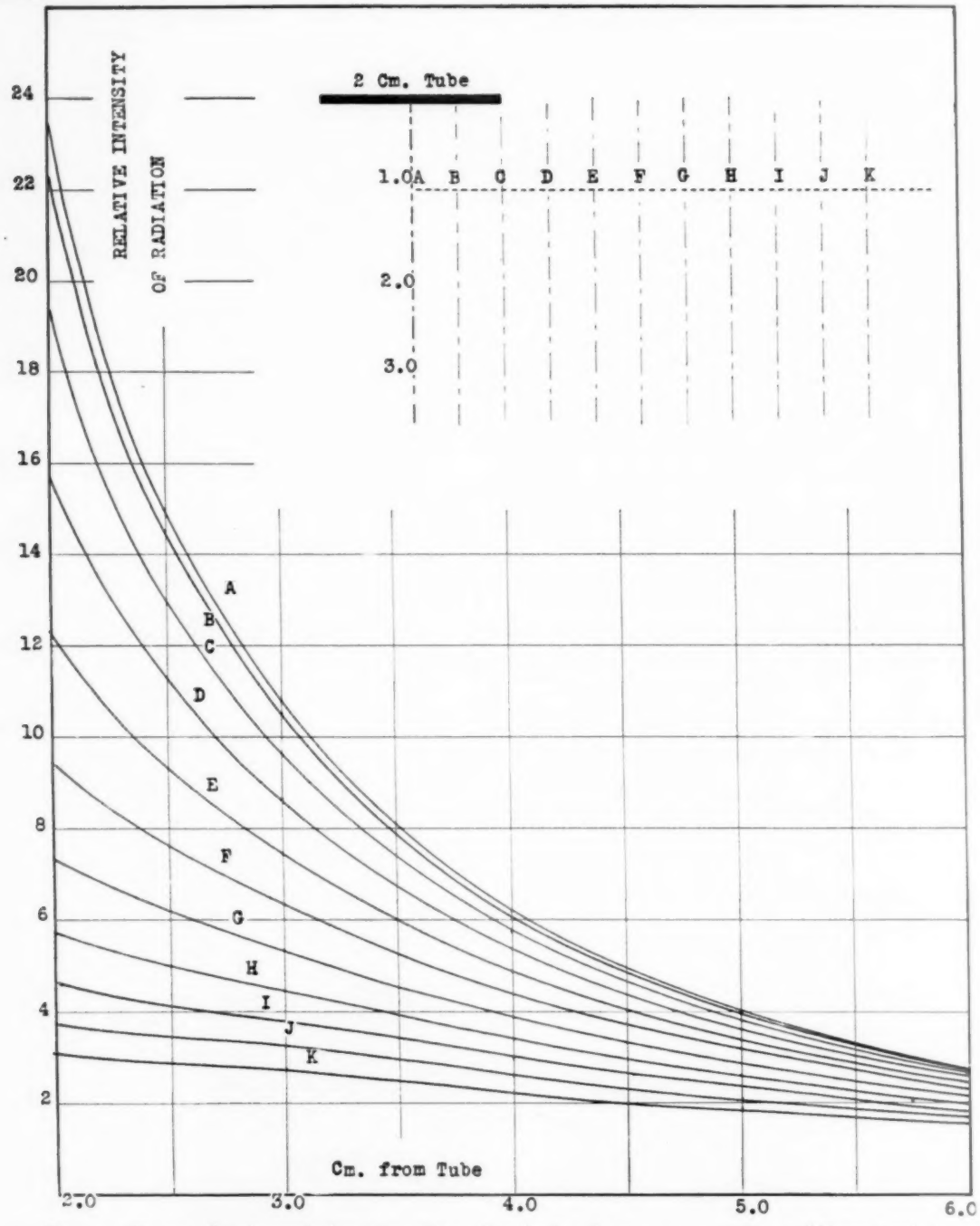


Fig. 3c. Curves showing relative intensities of radiation from a 2 cm. tube at different points.

In order to use such curves to determine the distribution of radiation on the skin under a given applicator, such a procedure

skin, and X, Y, and Z three points on the skin under the tube. X being directly under the center, its intensity will be found on

curve A, at the 3 cm. distance. Similarly Y, under the end, and 1 cm. from X, refers to curve C, and Z, 3 cm. out, to curve G. From these curves in Figure 3c the intensities at these points are in the ratios of 10.8, 9.7, and 5.3 respectively. If the line XYZ were not directly under the tube, but to one side of it, the distance would be greater, and would be found arithmetically. For instance, if it were 2 cm. to the side the distance would be $\sqrt{3^2+2^2}=3.61$ cm.

By such a method the relative intensities at different points on the skin due to any combination of tubes may be investigated. One example will be given in detail, and the results of a number of others.

When a small quantity of radium is available, an applicator frequently used is a 4×6 cm. pack carrying 5 tubes about 2 cm. long, arranged as shown in Figure 6A. This is most often used at a distance of 2 cm. from the skin. The distribution of radiation on the skin under such an applicator may readily be determined from the curves of Figure 3. Consider 12 points on the skin, as in Figure 6B. The distances from each point to each tube, along a perpendicular to the line of the tube, must be determined, and also on which curve the point falls, that is, its position relative to the tube (under its center, end, or farther out). Then the radiation intensity at each point due to each tube at its own distance can be read from the curves. The entire calculation for this particular applicator at a distance of 2 cm. is given in Table II. For each point, the first column gives the distance to the tube (the square root of the sum of the squares of the distance from the applicator to the skin and the distance along the skin perpendicular to the tube). The second column indicates the curve to be chosen, selected as indicated in Figure 5, and the third the reading from the proper curve at the indicated distance. The sum of the readings for the five tubes gives the radiation intensity at the indicated point, in terms of the arbitrary unit. The radiation at the central point may be called 100 per cent, and all the others calculated in terms of this, as indicated in the line marked Per Cent. Then if these percentages are plotted as in the curves of Figure 6, the relative intensities at any points along the lines I–IV, V–VIII, etc., can be obtained,—or the points at which definite percentages are delivered. Thus 90 per cent is found 1.2 cm. beyond I on the line between I and III; 80 per cent at 1.8 on this line I–III, and at 1.6 cm. beyond V on the line V–VII. In this manner the entire area may be charted as shown in the lower diagram on Figure 6. Evidently for this particular case the distribution is far from uniform. A small central area is fairly well irradiated, but toward the ends of the applicator the intensity is only half as great as

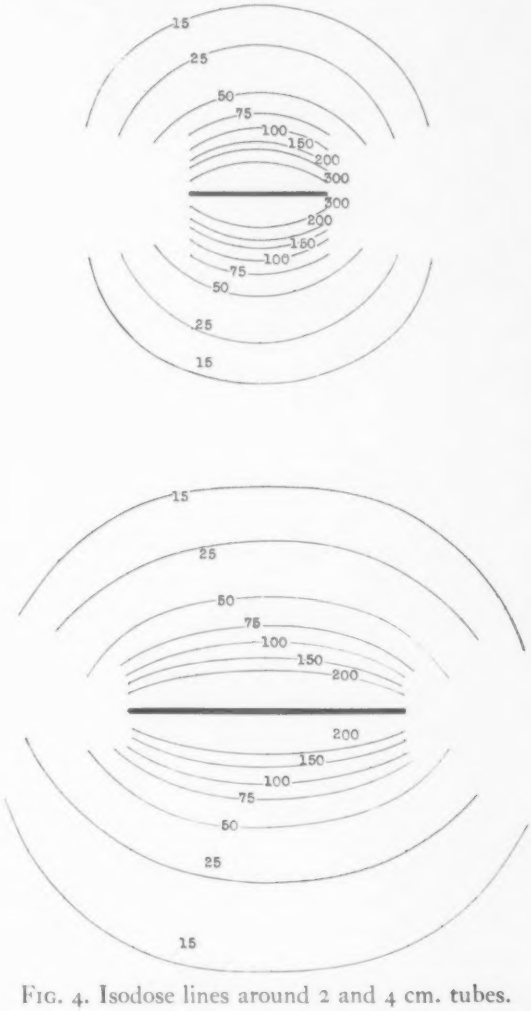


Fig. 4. Isodose lines around 2 and 4 cm. tubes.

TABLE II

DISTRIBUTION OF RADIATION INTENSITY UNDER A 4×6 CM. PACK 2 CM. FROM SKIN, CARRYING 5 EQUAL TUBES EACH 2 CM. LONG*

Tube	Point I			Point V			Point IX		
	Dist. cm.	Curve	Intensity	Dist. cm.	Curve	Intensity	Dist. cm.	Curve	Intensity
1	2.50	D	11.3	2.06	D	15.0	2.06	D	15.0
2	2.50	D	11.3	2.06	D	15.0	2.06	D	15.0
3	2.00	A	23.4	2.24	A	18.4	2.83	A	12.0
4	2.50	D	11.3	3.20	D	7.8	4.04	D	5.3
5	2.50	D	11.3	3.20	D	7.8	4.04	D	5.3
Total			68.6			64.0			52.6
Per Cent			100			93			77
	Point II			Point VI			Point X		
1	2.50	B	14.4	2.06	B	21.0	2.06	B	21.0
2	2.50	F	7.6	2.06	F	9.2	2.06	F	9.2
3	2.00	C	19.3	2.24	C	15.5	2.83	C	10.6
4	2.50	B	14.4	3.20	B	9.3	4.04	B	5.9
5	2.50	F	7.6	3.20	F	5.9	4.04	F	4.3
Total			63.3			60.9			51.0
Per Cent			92			89			74
	Point III			Point VII			Point XI		
1	2.50	B	14.4	2.06	B	21.0	2.06	B	21.0
2	2.50	H	5.0	2.06	H	5.6	2.06	H	5.6
3	2.00	E	12.3	2.24	E	10.6	2.83	E	8.0
4	2.50	B	14.4	3.20	B	9.3	4.04	B	5.9
5	2.50	H	5.0	3.20	H	4.2	4.04	H	3.4
Total			51.1			50.7			43.9
Per Cent			74			74			64
	Point IV			Point VIII			Point XII		
1	2.50	D	11.3	2.06	D	15.0	2.06	D	15.0
2	2.50	J	3.4	2.06	J	3.7	2.06	J	3.7
3	2.00	G	7.3	2.24	G	6.8	2.83	G	5.6
4	2.50	D	11.3	3.20	D	7.8	4.04	D	5.3
5	2.05	J	3.4	3.20	J	3.1	4.04	J	2.6
Total			36.7			35.4			32.2
Per Cent			54			52			47

*See Figure 6.

at the center. The situation would be improved by using more tubes. If more tubes are not available, a smaller area should be irradiated at one exposure, if the distance of the applicator is to be kept the same. Increasing the distance will improve the distribution of the radiation, but will also, of course, increase the time necessary to deliver a specified dose. In other words, if a given applicator is found to supply poorly distributed radiation, there are three possible ways to improve the situation: (1) Irradiate a smaller area at a time; (2) use more tubes in the applicator; (3) increase the radium-skin distance. These three possibilities will be considered in succession.

(1) Irradiate a smaller area at a time. If the same 5 tubes are distributed on an applicator just half the size of the first, namely 3×4 cm., as shown in Figure 7A, the distribution of intensity on the area underneath is that of Figure 7B. This is not appreciably better than that under the middle portion of the 4×6 cm. applicator. However, the intensity under the central point is 91 units instead of the 69 of Figure

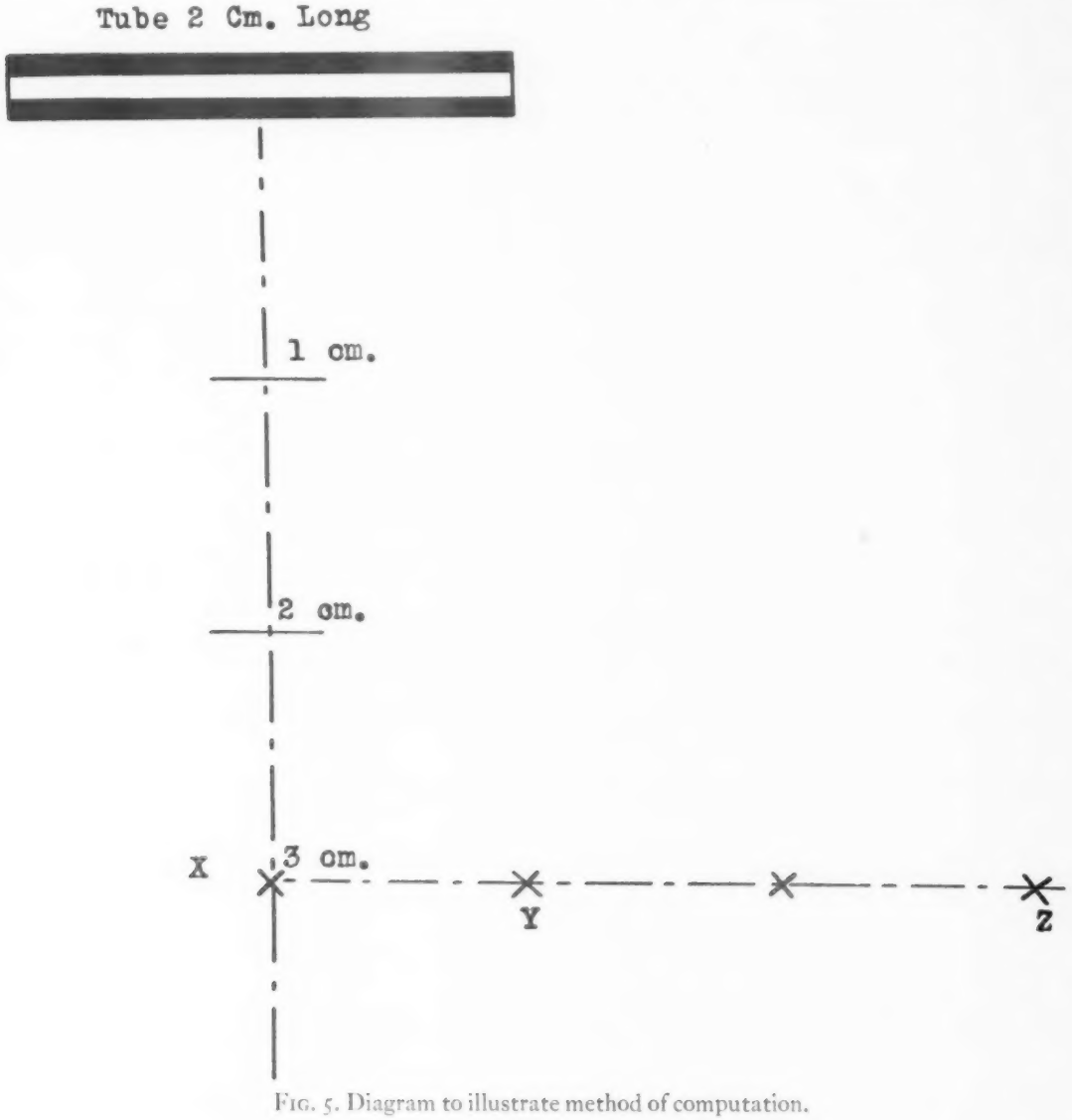


Fig. 5. Diagram to illustrate method of computation.

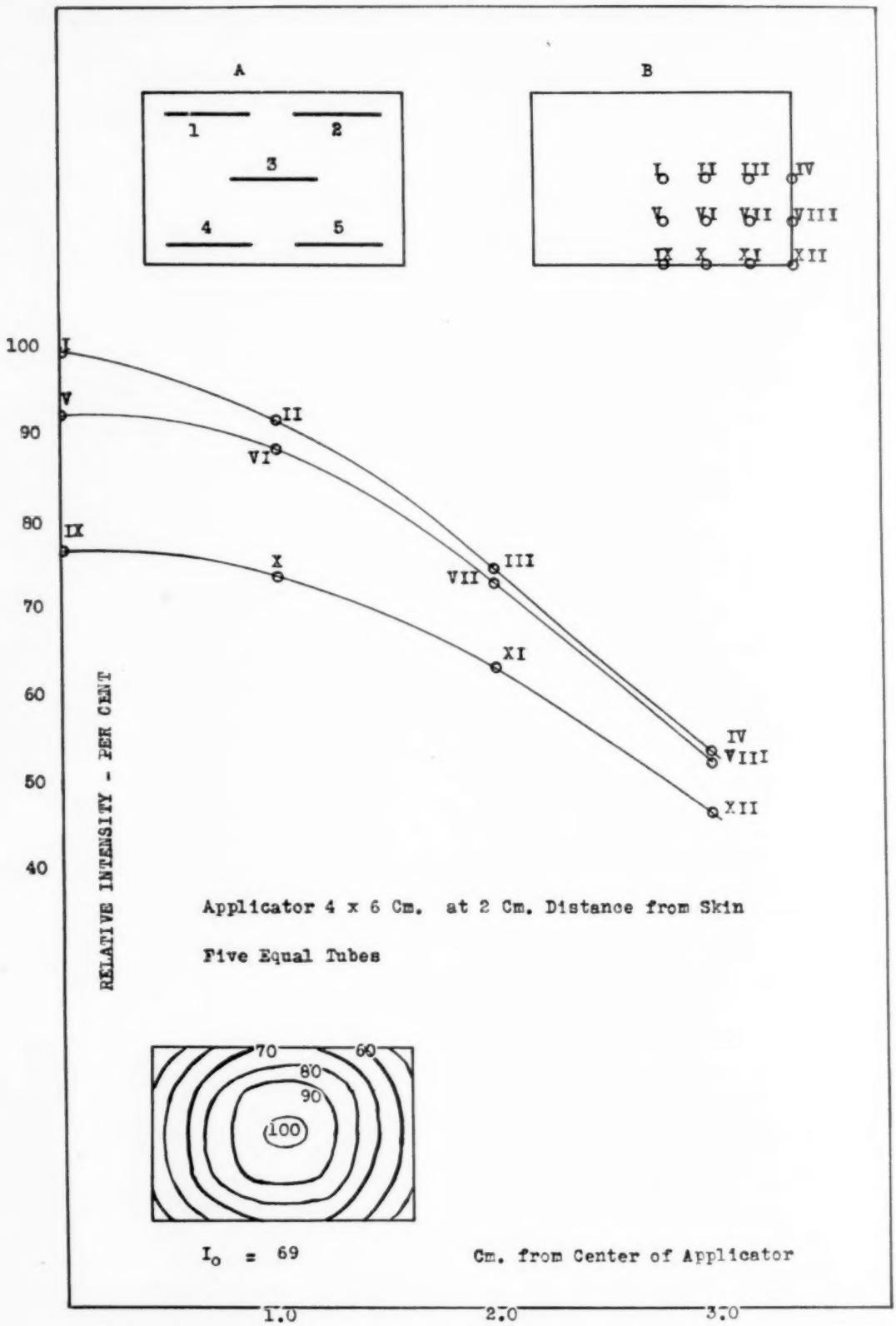


FIG. 6. Diagram showing computation of intensity chart data for a particular applicator. (To be used in conjunction with Table II.)

6, which means that to deliver the same dose at this point would require only 69/91 or 76 per cent as long a time. Of course, as just stated, a smaller area is receiving full benefit of the irradiation. If it is necessary to treat a larger area another application will have to be made over an adjacent field. In this case it is possible to calculate the radiation delivered over the second field by the applicator in the first position. Figure 7D shows the distribution of intensity over an area treated by the adjacent applications of the small applicator. In this case the intensity under the central point of the combination is 129 units. That is, it will deliver at this point the same dose as the first applicator in 54 per cent of the time. This means that the smaller applicator, used twice, each time 54 per cent as long as the larger one in its single treatment, or a total of 108 percent as much radiation, will deliver the same intensity at the center of the field as in the chart of Figure 6, and will at the same time, irradiate the whole field in the much more desirable manner of Figure 7D. It may be simpler to follow this argument with a specific quantity of radium. Suppose each tube to contain 10 mg., and the time for the 4×6 cm. applicator with 5 tubes (50 mg.) to deliver 1 erythema dose under its center at a distance of 2 cm. to be 20 hours. Then the half size applica-

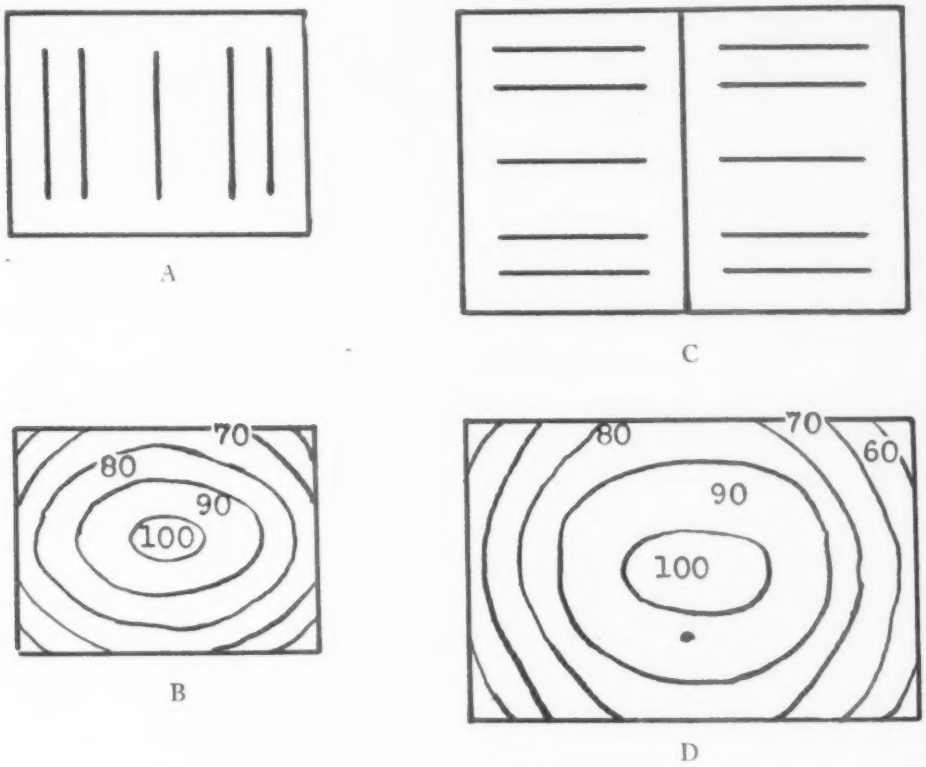


Fig. 7. Intensity charts for applicators of two sizes and strengths at 2 cm. distance from skin.

tor with the same 5 tubes will deliver the same dose under its center in 76 per cent of 20, or 15.2 hours. (Of course the skin 3 cm. from this point receives much less radiation than with the larger applicator.) Now, in order to treat the same area with the smaller applicator, two treatments are necessary, but in this case, due to cross-firing on one area from the other treatment, the time to deliver the same dose at the center of the area is 54 per cent of 20 hours, or 10.8 hours for each treatment, giving a total of 21.6 hours. This means that, by means of a rearrangement of sources and an additional hour and a half of treatment, a great improvement has been made in the uniformity of the radiation over the given area.

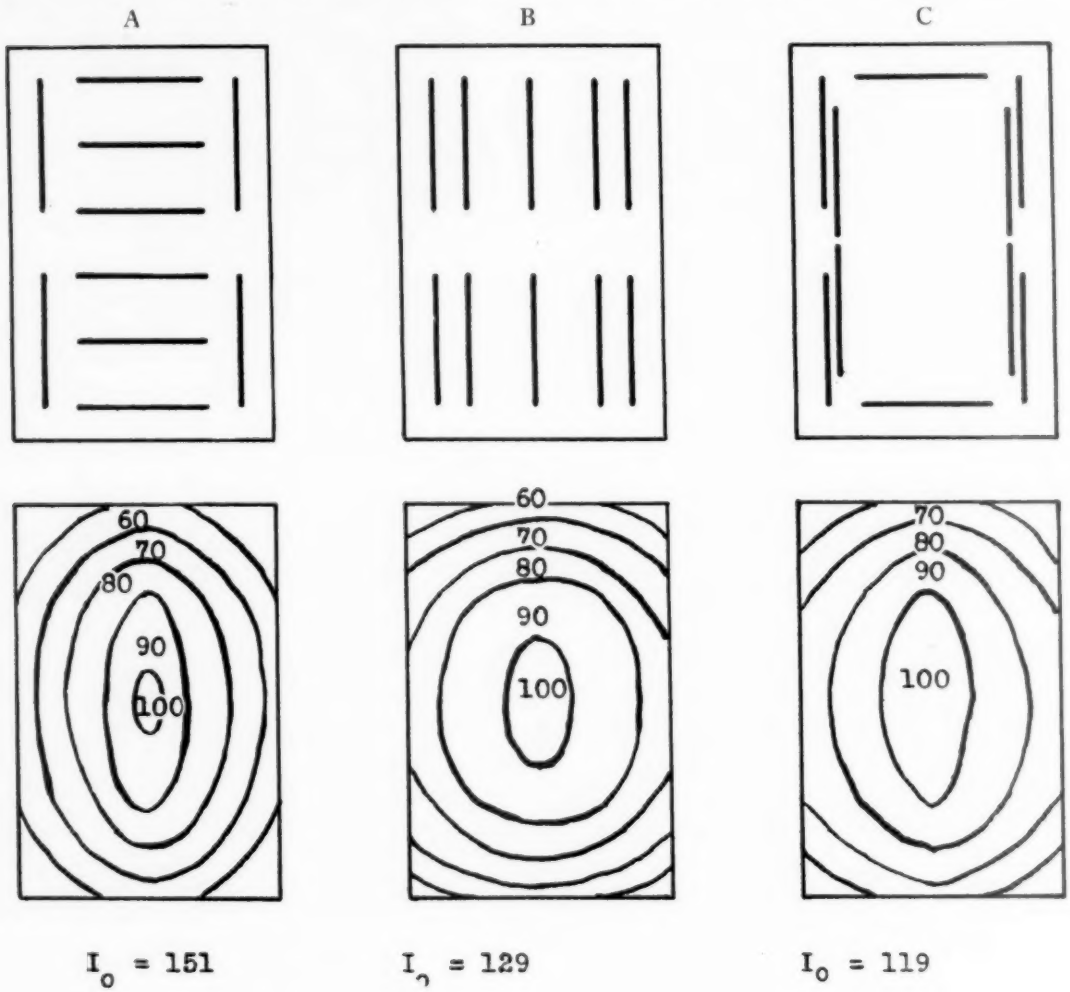


FIG. 8. Intensity charts for three arrangements of the same tubes on a 4×6 cm. pack 2 cm. from skin.

The point may here be made that placing a few widely separated sources on a large surface does not achieve the same end as having a large uniformly radiating surface. It is true that, for any given radium-skin distance, as the area of the source increases

while the distribution of radioactive matter remains uniform, the radiation on a field directly beneath it becomes more nearly uniform. A surface with many tubes close together may approximate a uniform surface, but when the tubes are at all widely spaced, the result is as just demonstrated. Therefore it is of no advantage, but rather the contrary, to use a large applicator if only a few tubes are available.

(2) Use more tubes in the applicator. With ten tubes available instead of five, considerable improvement is possible in the use of the 4×6 cm. applicator. The question at once arises as to the best manner of distributing these tubes in the pack.

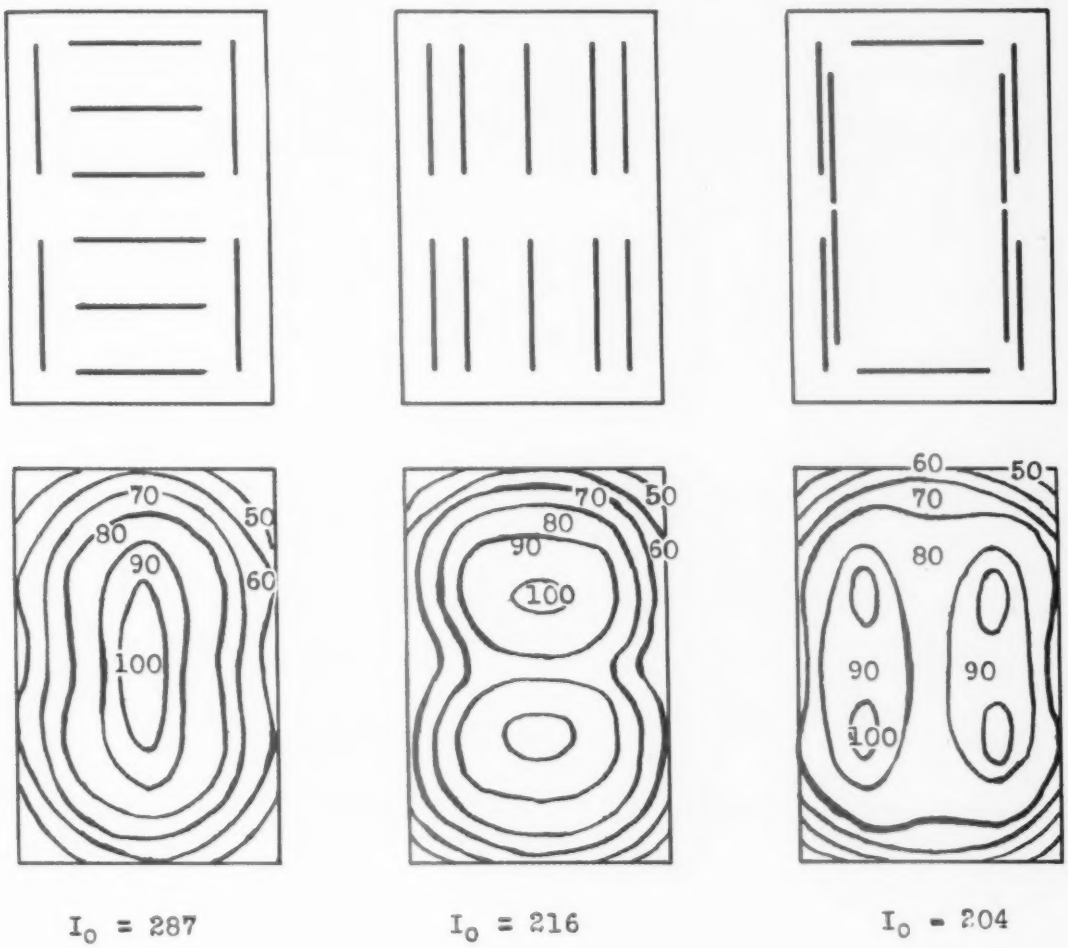


FIG. 9. Intensity charts for three arrangements of the same tubes on a 4×6 cm. pack 1 cm. from skin.

A number of possibilities suggest themselves. First, of course, is the arrangement corresponding to the two smaller applicators side by side. This is shown in Figure 8B. (It is, of course, the same as 7C.) Another arrangement which is often used, and which looks reasonable, is given in Figure 8A. The arrangement of Figure 8C does not

look so favorable as the others, but after a number of trials it was found to give the best distribution of intensity with an applicator of this size and ten tubes. That is, in this case, the tubes should be placed around the edges, rather than being spread over the whole pack. The figures also show the importance of finding a good arrangement. That of A gives a distribution of intensity on the skin which is little, if any, better than that with five tubes in Figure 6, though of course it delivers the required dose in a much shorter time. On the other hand, the arrangement of C gives a very much better distribution.

It must be borne in mind in studying these distribution charts that 100 per cent does not represent the same absolute value for the intensity in each case, but simply the maximum for each applicator. This maximum will, of course, vary with the arrangement of the tubes, and for this reason it is given, as I_0, for each case, in terms of the arbitrary unit. The times of irradiation

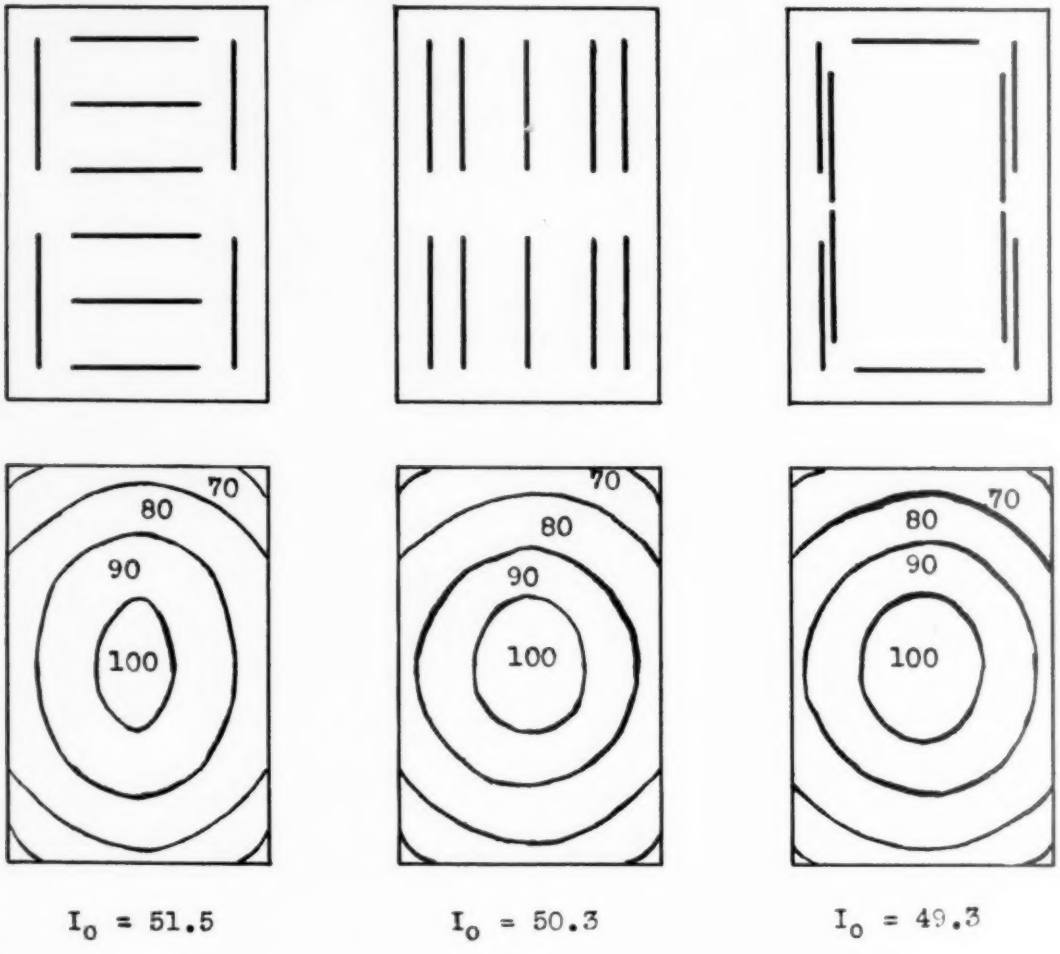
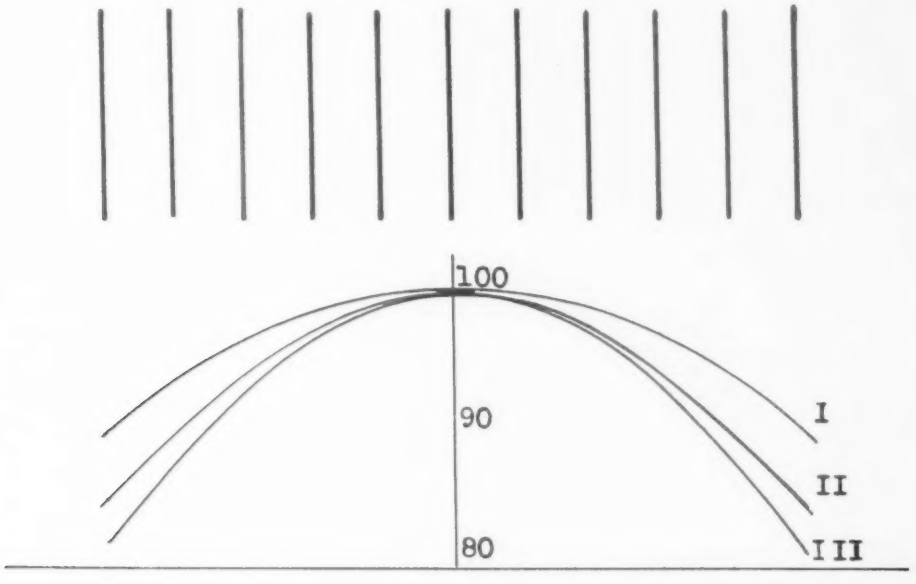


FIG. 10. Intensity charts for three arrangements of the same tubes on a 4 × 6 cm. pack 4 cm. from skin.

necessary to deliver the same doses at the center of the field are inversely proportional to these values for I_0. That is, it is necessary to increase the actual amount of radiation to deliver a given dose as the distribution is improved. For example, the I_0 for A, Figure 8, is 151 units, that for C is 119 units. Therefore it will require for the arrangement of C, 151/119 times as long as for that of B, to deliver an erythema dose under its center. But by using this additional time, it is possible to deliver to points outside the center, considerably greater doses.

(3) Increase the radium-skin distance. In Figures 9 and 10 are given distribution charts for the same three arrangements of ten tubes as in Figure 8, for 1 and 4 cm. distances. Comparison of these shows the great improvement in distribution with increase in distance, for any given arrangement of sources. Of course it must be remembered that increasing the distance increases the time necessary to deliver a specified quantity of radiation, so that there are practical limits to this method of improving the intensity distribution in any given case.



I - Eleven Tubes of Equal Strength

II - Tubes in Ratios 6-5-4-3-2-1-2-3-4-5-6

III - Tubes in Ratios 48-24-12-6-3-1-3-6-12-24-48

All Tubes 2 Cm Long, 0.5 Cm Apart, 4 Cm from Skin

FIG. 11A. Curves showing distribution of intensity under equally spaced tubes of different strengths.

It is evident from the above considerations that any particular applicator and combination of tubes constitutes an individual problem as regards the most effective and efficient method of treatment with it.

With larger applicators and more tubes, such calculations as those given above become very laborious. Yet it is important to know the best arrangements in these cases also. From this point of view it is of interest to find the best spacing for a row of

parallel tubes, so that, if possible, the radiation along a line under their centers should be uniform. Obviously if the tubes are of equal strength they cannot be equally spaced, for in this case the center would receive much the greatest intensity. Therefore they should be placed closer together toward the ends of the row, and farther apart in the center. If equal spacing is to be used for tubes of varying strengths, the stronger ones should be placed toward the ends. A combination of these two methods of arrangement may be used to advantage. The effect of spacing, with tubes of equal strength, is shown in Figure 11A. Curve I indicates the distribution of intensity under the center of a row of 11 equal tubes 2 cm. long, evenly spaced 5 mm. apart, at a distance of 4 cm. from the skin. In curve II, the tubes increase uniformly in strength from 1 at the center to 6 at the ends. In curve III, the end tubes are 48 times as strong as the center one (the strengths are in the ratios 1–3–6–12–24–48). It is evident from these curves that it is impossible, within practical limits, to make the radiation distribution actually uniform, but it is possible to reduce the variation to

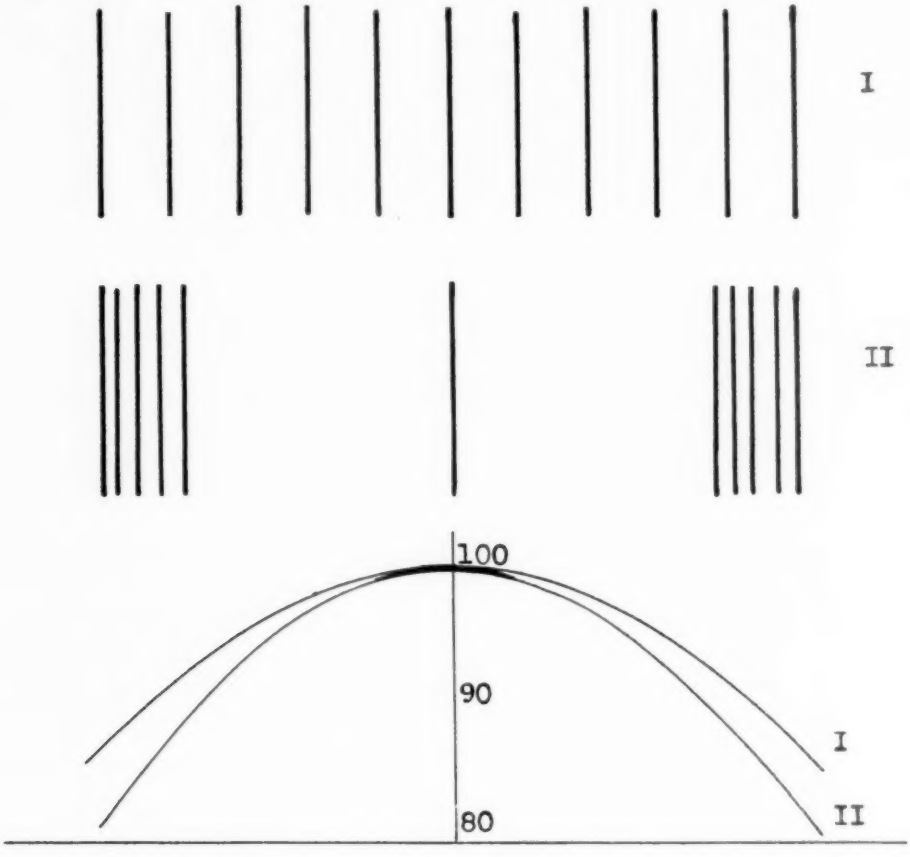


Fig. 11B. Curves showing distribution of intensity under differently spaced tubes of equal strengths.

a maximum of about 10 per cent. With regard to the problem of spacing tubes of equal strengths in the most advantageous manner, Figure 11B shows the distribution of intensity for uniform spacing, and for an arrangement with all the tubes except one crowded close to the two ends. In this case, as in the one just discussed, it is impossible to attain actual uniformity. The same situation will hold for longer distances, although as the distance increases the variation becomes less. For short distances the situation is somewhat different. When the distance from the applicator to the skin is comparable with the distances between the tubes, regions of greater intensity will lie under each tube, those of less intensity between them. However, for such short distances this problem is relatively unimportant. Small applicators will be used and the distribution can be found as described earlier in the paper.

In all the examples up to this point, 2 cm. tubes have been considered merely for convenience, since it was not thought advisable to include in this paper the actual curves for tubes of various lengths. They may easily be made from the data of Table 1. Similarly, in general, tubes of equal strength have been considered for any specific applicator. If tubes of different strengths are used, this may be allowed for in such calculations as those of Table 11 by multiplying the partial intensity due to each tube by a factor representing the strength of that tube, before the addition is performed. It sometimes happens that it is desirable to compare tubes, or especially needles, having the same strength per centimeter of length. In this case Table 1 can be adapted for ready reference, by a simple arithmetical transformation. The values for the point source and for the 1 cm. tube remain the same, those for the 2 cm. tube are multiplied by two, for the 3 cm. tube, by three, and so on.

The number of individual problems which may be attacked by this method is endless. Since each one necessitates rather extensive mathematical computations, it is impossible to give many in such a report as this. One more rather important one may be mentioned specifically,—it has been accepted implicitly in connection with the other examples. It is possible by means of these data to determine the dose for any external applicator (having a filter of approximately 0.5 mm. of gold or 2 mm. of brass), provided the dose for any other is known. For this purpose it is only necessary to calculate the intensity under the center of each applicator in terms of the unit used in Table 1; then the doses are inversely in proportion to these intensities. For instance, in Figures 7B and 8C the intensities are 91 and 119 respectively. If it is known that the first will produce an erythema with 1500 mg-hr., then the second will do so with 91/119 or 1150 mg-hr. For such dosage comparisons or determinations it is not necessary that the two applicators be of the same shape or size or be used at the same distance. All these variables are automatically allowed for in the determination of the I_0's.

A similar method of studying radiation intensities or dosages could be used in connection with the very large fitted wax applicators used in some clinics. In these cases great care would be necessary in calculating the distances and in determining which curve to use (center, end of tube, etc.).

For some purposes it would be advantageous if certain general relations could be found between the size of the tube or applicator, the distance from the skin, and the intensity of radiation delivered at various points. This has already been done in a previous paper for points directly under the center of applicators having uniform radiating surfaces.[7] If it were possible to find such an expression for the intensity under different parts of a tube, it would simplify the accumulation of further data of the sort here presented. To a certain extent this can be done from the data of Table 1. Consider a tube of length a, at a distance of a from the skin,—that is, a tube 1 cm. long at 1 cm., one 2 cm. long at 2 cm., etc.,—and relate the intensity of its radiation to that

TABLE III

EXAMPLE TO ILLUSTRATE METHOD OF FINDING RELATION BETWEEN INTENSITY OF RADIATION FROM ANY TUBE AT ANY DISTANCE, AND INTENSITY OF RADIATION FROM A POINT SOURCE AT THE SAME DISTANCE

Length of tube "*a*" cm.	Intensity from point source at distance "*a*"	Intensity from tube of length "*a*" at distance "*a*"	Ratio
1.0	100.00	93.5	0.935
2.0	25.00	23.41	0.935
3.0	11.11	10.36	0.932
4.0	6.25	5.77	0.926
5.0	4.00	3.57	0.920
		Average	0.930

TABLE IV

INTENSITY OF RADIATION FROM A TUBE OF LENGTH "*a*" AT POINTS IN DIFFERENT POSITIONS RELATIVE TO THE TUBE, AND AT DIFFERENT DISTANCES, IN PERCENTAGES OF INTENSITIES FROM POINT SOURCE OF SAME STRENGTH AT SAME DISTANCES

Distance in terms of "*a*"	Radiation Intensity Per Cent of Intensity from Point Source at Same Distance						
	Under Center	Half-way to End	Under End	¼ "*a*" beyond End	½ "*a*" beyond End	¾ "*a*" beyond End	"*a*" beyond End
0.25	56	51	33	12	6	4	2
0.50	79	72	53	33	20	13	9
0.75	87	82	68	50	35	26	19
1.00	93	89	77	62	49	38	29
1.25	95	92	83	71	59	48	39
1.50	97	96	87	78	67	57	48
1.75	98	97	90	82	73	64	54
2.00	98	98	92	86	78	70	62
2.25	99	98	94	88	82	75	67
2.50	99	99	95	90	85	78	71
2.75	99	99	96	92	87	81	75
3.00	99	99	96	93	88	83	78
3.5	99	99	97	94	90	86	82
4.0	100	99	98	95	92	87	84
4.5	100	100	98	96	93	89	86
5.0	100	100	99	97	94	90	87

from a point source of the same strength, at the same distance. This is done in Table III. Column 1 gives various lengths of tube, considered in turn as *a*. Column 2 gives the relative intensities from the point source at these distances. In column 3 are the readings from Table I for the intensity under the center of each tube at a distance of its own length *a* from the skin. In the last column are the ratios between the intensity for the tube and for the point source at the same distance. Since these ratios are practically the same, it may be concluded that their average, 0.93, represents the ratio between the intensity of radiation from any tube (within reasonable limits) at a distance of its own length from the skin, and a point source of the same strength at the same distance from the skin. In a similar manner it may be shown

that for a tube of length a at a distance of $2a$, the intensity is 0.98 of that from the point source at the same distance, and for a tube of length a at a distance of $0.5a$, it is 0.79 of that from the point source at that distance $2a$, 0.979, at distance 0.5 a, 0.778.

In the same way may be obtained the intensities for points under the end of the tube, or in any other position relative to it. This is done in Table IV, for a tube of

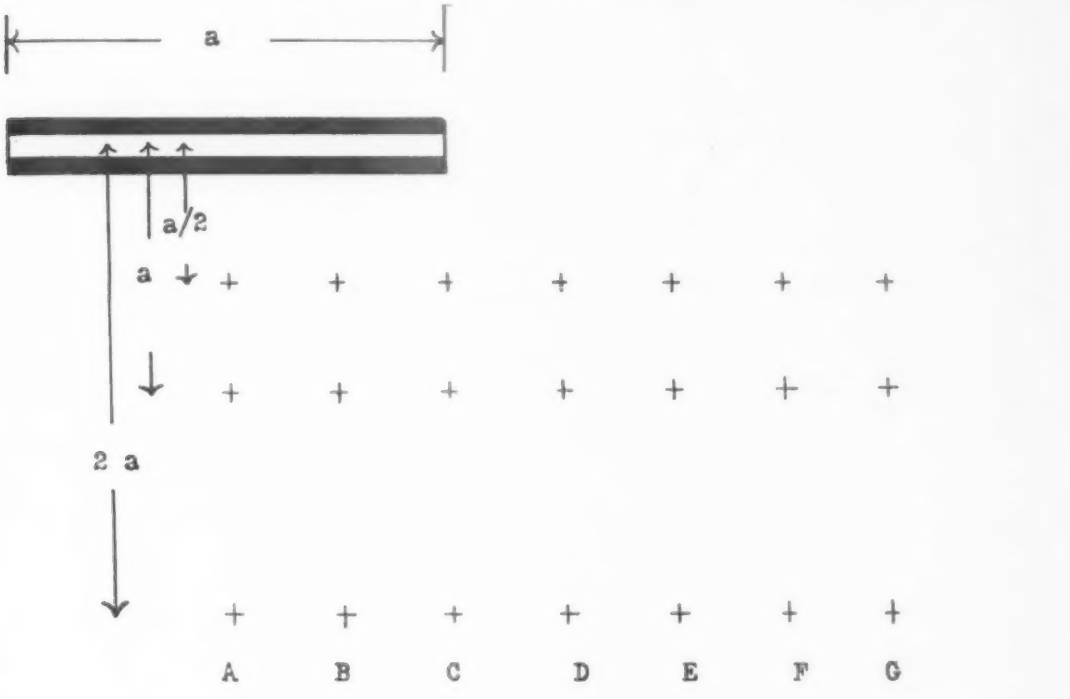


FIG. 12. Points for which intensities were computed for the general relation.

distance. In the paper just referred to, as stated above, these data are given for points under the center of the applicator. They were calculated in a somewhat different manner, but they agree very well with those just derived. For the tube of length a at distance a, they give 0.923, at length a, and points as shown in Figure 12. By this means the entire data of Table I are reduced to a very compact form. From it, for any specific case, the numerical data can be obtained. As an example, the data for the 2 cm. tube will be calculated, although this has already been given in

TABLE V

CALCULATION OF DATA FOR 2 CM. TUBE

Distance		Radiation Intensity							
Cm.	"a"	From Point Source	From Tube						
			Under Center	Half-way to End	Under End	Out 0.5 cm.	Out 1.0 cm.	Out 1.5 cm.	Out 2.0 cm.
0.5	0.25	500	224	204	132	48	24	16	10
1.0	0.50	100	79	72	53	33	20	13	9
1.5	0.75	44.4	39	36	30	22	16	12	8
2.0	1.00	25.0	23	22	19	16	12	10	7
2.5	1.25	16.0	16	15	14	12	10	8	6
3.0	1.50	11.1	11	10	9	8	7	6	5
4.0	2.00	6.25	6	6	6	5	5	4	4
5.0	2.50	4.00	4	4	4	4	3	3	3
6.0	3.00	2.78	3	3	3	3	2	2	2
Point for Verification from Table I			A	B	C	D	E	F	G

Table I, in order that the calculations may be easily verified. They are given in Table V. Each column is obtained by multiplying the value for the intensity from the point source at each distance by the corresponding factor from Table IV. These values should be the same as those for the 2 cm. tube in Table I. The corresponding points of Table I are given at the bottom of Table V for comparison. The slight discrepancies are due to the fact that the factors in Table IV are obtained from averages of several from Table I.

A table similar to V can be constructed for any desired tube. From the data thus obtained, curves similar to those of Figure 4 may be drawn, for calculations of the sort demonstrated earlier in the paper; or, for approximations, values may be obtained directly from the tables, by interpolation. Thus the scope of the material here presented is extended to any tubes likely to be met with in practice.

The author wishes to acknowledge her indebtedness to Dr. Failla, who suggested the problem, for his helpful comments during its development. She also wishes to thank Miss Dorothy Applegate and Mr. Steven Suozzi for their assistance in making some of the computations.

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DISCUSSION

Dr. J. L. Weatherwax, Philadelphia, Pa.: We certainly are much indebted to Mrs. Quimby for giving us a method of arranging radium tubes in plaques, and I was especially interested in the arrangement of the tubes between 2×3 and 4×6. I think the curves and tables Mrs. Quimby will show in her publication will be of much assistance to the radium therapist in making up the plaques and packs for treatment.

Dr. Otto Glasser, Cleveland, Ohio: Mrs. Quimby's paper on the distribution of radiation intensity around various radium preparations and combinations of preparations is excellent and fills a definite need. It is interesting to see the development which this problem has gone through since the time almost fifteen years ago when I first determined the curves of equal intensity around radium capsules at the Freiburg University together with my teacher Professor Friedrich, at which time we coined the word "Isodoses."

THE ROENTGEN TREATMENT OF AGRANULOCYTOSIS

REPORT OF TWO CASES WITH RECOVERY

By LESLIE T. GAGER, M.D., *and* ALMA JANE SPEER, M.D.
WASHINGTON, D.C.

HOW Friedemann, in his work with agranulocytosis in the division of infectious diseases of the Rudolf Virchow Krankenhaus, turned for help, in 1927, to the roentgen ray, after an unbroken series of deaths in patients treated by conventional modes of therapy, is now a familiar story.[3] The latest report of Friedemann and Elkeles[4] shows the recovery, under the stimulating influence of roentgen irradiation of the long bones, of 13 out of 15 uncomplicated cases, although at the same time it is made clear that treatment is hopeless when a secondary general sepsis or pneumonia supervenes (23 such patients died), while 5 other patients died within thirty-six hours after the first irradiation.

In support of the value of roentgen therapy for agranulocytosis and granulopenia have come reports from an increasing number of workers. In this country Call, Gray and Hodges[1] reported the successful use of roentgen treatment in 1928, after two transfusions had been without result. Waters and Firor,[7] in 1931, reported 4 out of 5 patients living after roentgen-ray exposure, although the use of other measures of treatment in all their cases qualified the specific evaluation of irradiation. Most recently Taussig[6] has recorded prompt and satisfactory responses to roentgen treatment in 4 patients, although later 2 of these had relapses, were found refractory to roentgen radiation, and died in coma. Furthermore, though cures which are spontaneous or due to other measures are reported,[2] Taussig's analysis of 340 cases of agranulocytosis—with a mortality of 79 per cent—shows a death rate of 53 per cent only in the group of 80 patients treated by irradiation of the long bones. By contrast, of 49 patients treated by transfusion, 69 per cent died; of 31 patients who were given neoarsphenamine, 77 per cent died, and the mortality was 75 per cent among the 172 patients who received treatment by other methods.

To add to the evidence in favor of irradiation from a case of agranulocytosis in which it was the sole specific method of treatment and also to point out its value in the recurrent as well as primary attack, we report our experience with a patient whose blood on four occasions within a period of ten weeks showed a total absence of granulocytes. Coming under our observation soon after we had read Roberts and Kracke's[5] dramatic account of the physical collapse and immunologic failure which in their patient were the prompt sequelae of the disappearance of the polymorphonuclear cells from the blood stream, our much younger woman seemed about to become the victim of a similar chain of events. We are convinced by the clinical facts that the timely use of irradiation was the deciding factor in her recovery from the four crises.

A similarly happy result has also been witnessed in one other patient following roentgen treatment and brief mention of this case is made through the courtesy of Dr. G. R. Huffman.

CASE REPORTS

CASE 1. Irene G., colored, aged twenty-four, married, employed as a domestic, was admitted, by ambulance, to the George Washington University Medical Service, Gallinger Municipal Hospital, on December 2, 1930. The patient was so weak as to be almost unable to speak. The chief complaints were pain in the chest of two days' duration and sore throat and mouth of ten days' duration.

The present illness began about November 15, 1930, with aching of the teeth "like neuritis." On November 21 extraction of the left upper central incisor was followed by swelling and pain in the gums and gradual extension of an inflammatory process to the whole mouth

and throat. Sharp pains in the right upper chest began on December 1.

The patient's mother and father are living and well; she has two brothers and four sisters, all living and well, and has a maternal grandmother who is well at the age of eighty-four. Her childhood was one of good health, and sore throats were unknown until the present illness.

In March, 1929, after she had given birth to an apparently healthy child, the patient's blood Wassermann test was found positive. Treatment was irregular for a year but on February 1, 1930, she came under observation at the city health station. Between this date and November 13, 1930, she received eight intravenous injections of arsenobenzol (0.3 gm. each) and then eight intramuscular injections of mercury salicylate (0.065 gm. each). In addition, vaginal smears in February showed Gram-negative intracellular diplococci and thereafter topical applications of mercurochrome were made twice weekly to the cervix and the vagina was similarly swabbed.

On admission, December 2, the temperature was 104.5° F., pulse 124, respiratory rare 36. The patient lay in semi-stupor, undernourished, pale, with sclerae slightly icteric. The pupils were equal and responded to light.

The socket of the extracted incisor tooth was necrotic, there was an ulcer on the left tonsil, the tongue and palate were covered in places with a grayish-white membrane, on removal of which the underlying surface bled easily. The entire mucosa of the mouth and throat was red and swollen, pyorrhea was profuse and the lymph nodes of the upper neck were enlarged and tender. The epitrochlear nodes were palpable.

The right chest showed lagging, resonance was impaired over the base posteriorly and the breath sounds were diminished. There was a loud apical systolic murmur without evidence of cardiac enlargement. The blood pressure was 180/84 (later falling to 110/50).

In the left upper quadrant tenderness was present and a soft spleen was palpated.

Around the urethral orifice was an area of ulceration covered by whitish exudate and the whole vulva was red and inflamed.

At the base of the index finger of the left hand a deep ulcerated area was covered by a grayish-white membrane. Healed ulcers of long standing were present on both arms and legs.

There was no dependent edema. Deep reflexes in all extremities were overactive and there was clonus of the lower jaw.

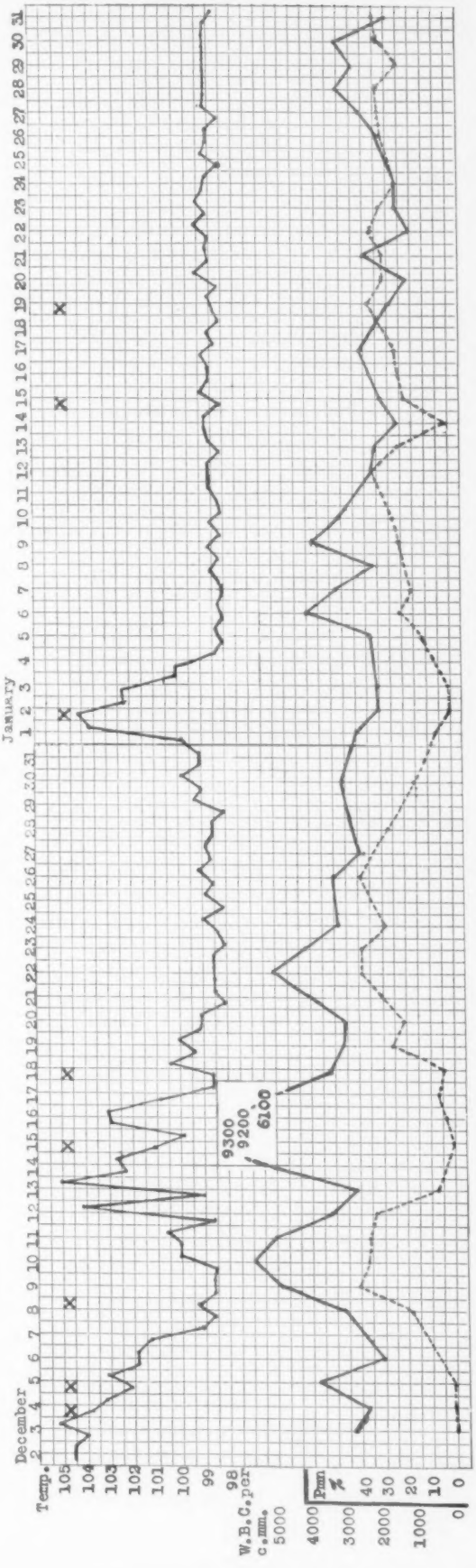

Chart 1. Showing the course of the temperature (solid line above), total white blood cells (solid line below) and granulocytes (broken line), in Case 1. Roentgen treatment is indicated by x.

The urine contained much albumin and urobilin. Vincent's organisms were found in smears from mouth, tonsils and the ulcers of vulva and hand.

Blood sugar was 118 mg., urea nitrogen 15 mg. The van den Bergh direct reaction showed an immediate color change, indirect 2.7 mg. per 100 c.c. of blood.

The first examination of the blood cells was on December 3: hemoglobin 60 per cent, red cells 4,710,000, leucocytes 2,900. The differential count showed polymorphonuclear neutrophiles, 0; lymphocytes, 62 per cent; mononuclears, 38 per cent; band forms 0. The subsequent course of the white count and neutrophiles is shown by Table 1 and Chart 1.

The problem of the treatment of agranulocytosis at once arose.

The immediately supportive measures of intravenous glucose-saline solution, adequate doses of digitalis and the local use of sodium perborate for the ulcerative lesions were without striking effect. On December 3 the areas of ulceration and necrosis were spreading, the temperature rose to 105.2° F., and the condition of the patient was obviously growing still more desperate.

On December 4 recourse was had to the roentgen ray. Irradiation was applied by Dr. J. K. Williams in approximately one-fourth of an erythema dose to the upper two-thirds of the left femur. The clinical response was immediate

TABLE I

DAILY BLOOD COUNTS IN AGRANULOCYTOSIS (CASE 1)

Date 1930	White Blood Cells	Differential						Comment
		Neu.	Lymph.	Mono.	Band	Young	Myelo.	
				Period of First Attack				Hb. 60%; R.B.C. 4,710,000.
12/3	2,900	0	62	38	0			Smears from throat positive for Vincent's organisms.
12/4*	2,100	1	70	29	0			Necrosis of gum, ulcer of tonsil, vulva and hand.
12/5*	3,800	1	70	29	0			
12/6	2,000							
12/8*	3,100	19	56	7	16	2		
12/9	4,900	40	33	15	10	2		
12/10	5,650	36	36	10	16		2	
12/11	5,000	36	45	10	9			
12/12	3,450	33	50	12	5			
				Period of Second Attack				
12/13	2,400	7	72	19	1		1	
12/15*	9,300	0	44	56	0			Bilateral otitis media.
12/16	9,200	4	44	52	0			
12/17	6,100	11	71	4	12	1		
12/18*	3,400	8	73	0	19		1	Mast Cell.
12/19	3,100	27	46	12	15			
12/20	3,000	21	46	3	30			1 Türck's irritation cell.
12/22	5,000	39	39	8	14			
12/23	4,200	39	37	5	19			
12/24	3,200	27	45	7	20		1	
12/26	3,300	39	53	3	5			
12/27	2,600	38	49	6	7			Right tonsil covered with grayish membrane.
12/28	2,750	26	54	6	14			Streptococcus isolated from throat.
12/30	3,000	15	75	5	5			Hb. 60%; R.B.C. 3,280,000.
1931 1/1	2,600	6	81	10	3			

Table I (*Cont.*)

Date 1930	White Bloood Cells	Differential						Comment
		Neu.	Lymph.	Mono.	Band	Young	Myelo.	
				Period of Third Attack				
1/2*	2,000	0	86	14	0			
1/3	2,050	1	85	1	13			Right tonsil ulcerated.
1/5	2,250	12	71	4	13			
1/6	4,000	20	74	0	6			
1/7	3,150	16	69	7	8			
1/8	2,300	30	60	6	4			
1/9	3,700	20	64	16	0			
1/10	3,000	24	60	6	8		2	
1/12	2,100	32	65	1	2			
1/13	2,000	22	64	8	6			
				Period of Fourth Attack				
1/14	1,400	0	66	6	28			
1/15*	1,800	18	72	6	4			
1/17	2,350	22	70	7	1			Kahn test four plus.
1/19*	1,600	34	58	4	4			
1/20	1,200	26	63	5	6			
1/21	2,300	26	61	8	5			
1/22	1,000	32	60	4	4			
1/23	1,400	28	52	12	8			
1/24	1,400	22	62	4	12			
1/26	1,900	28	70	0	2			
				Period of Recovery				
1/27	2,400	28	66	0	6			
1/28	3,000	29	52	11	8			
1/29	2,600	20	72	0	8			
1/30	3,100	27	71	0	1			1 mast cell.
1/31	1,600	30	58	6	4			2 mast cells.
2/2	4,500	43	52	2	3			
2/3	3,600	35	65					
2/4	3,200	33	61	5				1 mast cell.
2/5	2,000	30	66	2	2			
2/6	2,000	28	54	10	8			
2/12	3,500	40	49	5	1			
2/13	4,600	39	50	7	4			
2/14	3,400	25	70	2	3			
2/27	5,200	59	49	2				
2/28	4,200	44	44	10	2			
3/2	4,500	43	52	2	3			

* Roentgen irradiation of long bones. Laboratory studies by Dr. H. H. Leffler and staff.

and remarkable. The temperature began to fall, along with pulse rate and respiration and the white count on the following day was 3,800. Dysphagia was less marked, the oral inflammation was subsiding and the patient was rational.

On December 5 the right femur was similarly irradiated and the clinical improvement continued. On December 7, there was an unfavorable relapse, glucose was given intravenously and a third application of roentgen rays fol-

lowed on December 8. The temperature now fell to normal, the neutrophiles rose to 40 per cent on December 9.

On December 10, the total white count reached 5,650 but the neutrophiles fell to 36 per cent. On December 11 and 12 there was a rise in temperature and suggestive bronchopneumonic signs in the right chest. The storm broke on the night of December 12 with a fever of 104.2° F., and a neutropenia of 7 per cent. In addition to the re-lighting up of the oral and vulval inflammation, there developed a bilateral otitis media. On December 15 there was a marked response of lymphocytes and mononuclear cells, 9,300 per c.mm., but neutrophiles were wholly absent.

Irradiation applied posteriorly to the legs terminated this third attack with prompt fall in temperature, healing of the ulcerated areas and subjective improvement.

Bone marrow response was more gradual and less sustained, for on January 14 the white count reached a new low level of 1,400 cells, granulocytes 0. There was a repetition of the bacterial invasion of throat and vulva, but much milder in degree, and interestingly enough, almost no febrile movement. The seventh and eighth doses of roentgen rays were given on January 15 and 19 to legs and arms respectively. Thereafter, during the six weeks' remaining stay in hospital, further irradiation was unnecessary. She was out of bed on January 21, gained weight on a high caloric diet, was an active helper in the ward and was discharged on March 2. Her Wassermann reaction remained four plus.

TABLE II

SUMMARY OF ROENTGEN TREATMENT (CASE I)

Technique: 135 kv., 4 mm. aluminum filter; time, 8 minutes; distance, 40 cm., 5 ma.

Areas treated:	
December 4	(1) Upper left femur anterior.
December 5	(2) Upper right femur anterior.
December 8	(3) Lower anterior surface of both legs from knees down, 2 areas.
December 15	(4) Anterior surface of both arms from shoulders down, 2 areas.
December 18	(5) Anterior surface on both legs from hips to toes using 3 areas on each leg.
January 2	(6) Posterior surface of both legs from hips to toes, 3 areas on each leg.
January 15	(7) Anterior surface of both legs from hips to toes using 3 areas.
January 19	(8) Posterior surface of both arms from shoulders, including scapula to wrists, using 3 areas.

Again roentgen therapy was called upon and the arms were now irradiated, on December 15, followed by exposure of the legs on December 18. Once more, as the chart shows, the patient's response was prompt and favorable and there ensued a ten-day interval without fever, with subsidence of the local lesions and much gain in strength.

An ominous fall of the total white count and particularly of the neutrophiles began in the last days of December. In spite of this it was noted, on December 30, that "the patient seems very much improved, appetite good, sleeps soundly, cooperative and cheerful, up in chair for one hour." Subjectively December 31 was an equally comfortable day, but on the evening of January 1, 1931, the patient complained of "headache and a general bad feeling." The neutrophiles were now 6 per cent. On January 2, she was weak, had lost appetite and her complaint of sore throat was accompanied by ulceration both of the left tonsil and vulva: the white count was now 2,000, granulocytes 0. The temperature rose sharply to 104° F.

CASE II. N.H., a white girl, aged nineteen, a waitress, came into the Gynecological Service of Gallinger Municipal Hospital on February 8, 1930, with a vaginal discharge and a maculopapular rash over the face and trunk. She had had sore throat for two weeks, and three attacks of tonsillitis in earlier years.

The patient was afebrile, well developed and well nourished, and the only conspicuous physical finding was the rash, the nature of which was diagnosed as syphilitic. The blood Wassermann reaction was four plus. A vaginal smear showed no gonococci. The blood count on February 9 showed 7,800 white cells; polymorphonuclears, 62 per cent; lymphocytes, 24 per cent; eosinophiles, 5; band forms, 8; mast cells, 1 per cent.

Four intravenous injections of neoarsphenamine were given at weekly intervals, 0.4 gm. on February 11, 0.6 gm. on February 18, 0.9

gm. on February 25 and March 4. There were no unfavorable reactions, the skin eruption cleared, and the patient's condition was good.

On March 7, she again had sore throat, with headache, a fever of 102° F., and pains all over the body. The signs were those of acute follicular tonsillitis. The white count on March 8 was 3,700 with lymphocytes 70 per cent, mononuclears 29 per cent and polymorphonuclear cells 1 per cent. There were no polymorphonuclear leucocytes to be seen on March 9; the total count was 4,000, with 74 per cent lymphocytes, 24 per cent large mononuclears, one eosinophile, one basophile. Spirochetes and fusiform bacilli were seen in the throat smear; a blood culture remained sterile.

With no improvement from routine measures, the patient was given irradiation by Dr. Williams on March 13 over the upper part of the right femur and on March 14 over the upper left femur. The factors were: 135 kv., 5 ma., 4 mm. aluminum filter, 40 cm. distance, time 6 minutes.

Improvement was prompt and lasting. From a white count of 5,000, with one polymorphonuclear cell only on March 14, the count had risen on March 15 to 9,400, with polymorphonuclears 25 per cent, lymphocytes 24 per cent, large mononuclears 22 per cent. In this differential count there were also 5 per cent myelocytes, 8 per cent young forms and 14 per cent band forms of granulocytes.

There was prompt recession of the inflammatory lesions, the counts remained high and the patient left the hospital on March 28 with white blood cells 8,600 per c. mm., and a differential count of 58 per cent polymorphonuclears, 27 per cent lymphocytes, 5 per cent mononuclears, band forms 7, eosinophiles 2, mast cells 1 per cent.

COMMENT

Two cases of agranulocytosis, with recovery, are reported. Roentgen irradiation was the only general therapeutic agent employed in the crises of the disease.

While the clinical facts and the already rich literature make comment at any length unnecessary, there is offered, to our minds, unequivocal demonstration of the specific value of roentgen radiation in stimulating the production of granulocytes and of the vital importance of these cells to the body as a whole. Perhaps we can do no better than echo the thought of Friedemann that this surprising result of a minimal roentgen dosage in such a serious disease picture offers for analysis a roentgen-ray effect of great biologic interest, and not less important, the nature of the pathologic process which thus reverts to normal.

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THE EVOLUTION OF PULMONARY TUBERCULOSIS IN CHILDREN AS REVEALED BY THE ROENTGENOGRAM*

By HENRY D. CHADWICK, M.D.
Detroit Department of Health
DETROIT, MICHIGAN

IN ORDER to place the right interpretation on the densities caused by pulmonary tuberculosis and revealed by the roentgenogram, it is necessary to carry in one's mind a clear conception of the anatomical manifestations that take place following infection. A first infection of the lung with the tubercle bacillus is always followed by a similar sequence of events, regardless of the age of the individual when this infection takes place.

Because of the many opportunities for infection to which children are subjected, many of them are inoculated with the tubercle bacillus by the time they reach adult life. For that reason the disease that results is called the "childhood type of tuberculosis." The adult type of tuberculosis, from which it is important to differentiate it, is the result of reinfections. The childhood type may be found in adults who have escaped infection in childhood, and we may find the adult type in children where continued infection or reinfection has occurred soon after the development of the allergic and immune phenomena that are produced by the first infection.

When the tubercle bacillus is first implanted in the lung, the immediate response is the formation of a tubercle. About this an exudative infiltration develops, which is really a bronchopneumonia. This may vary in area from a focus of miliary size to the involvement of a whole lobe, depending upon the degree of tissue sensitivity and the number and virulence of the bacilli. At the center of the focus, caseation rapidly occurs, and about its periphery a capsule of fibrous tissue is formed. Almost simultaneously with the formation of the primary nodule in the parenchyma, the lymph channels draining the diseased area carry bacilli to the regional lymph nodes. In them occur exudation, caseation, proliferation and capsule formation. The nearest nodes are first diseased, and then because of imperfect walling off, others in the ascending chain along the bronchus and trachea become infected and diseased.

The progressive and retrogressive changes in the nodes follow the same course as in the primary focus in the lung. Retrogression of disease in the oldest lesions goes on with progressive disease in other nodes more recently infected. About the lesions in the parenchyma and in the tracheobronchial nodes, resorption of exudate occurs. A focus decreases in area, and in course of time the caseated center and the capsule about it become impregnated with calcium. Hard calcareous masses form, and in course of years even true bone formation may result. That is what happens in favorable cases. Rarely, however, the allergic reaction is so intense that the center of the pneumonic area undergoes rapid necrosis with liquefaction and the formation of a tuberculous abscess.

In other unfavorable cases, peripheral spread may occur with consequent invasion of the adjacent pulmonary tissue, or a hematogenous dissemination of bacilli to other organs takes place. General miliary or nodular tuberculosis, meningitis, or bone and joint disease may follow. The lesions caused by clinical primary tuberculosis as shown in the roentgenogram, therefore, may vary greatly in appearance according to the extent, location and phase of the disease at the time the film is taken.

* Read before the New England Roentgen Ray Society, Boston, Mass., January 16, 1931, and the Detroit Roentgen Ray Society, Detroit, Mich., February 5, 1931.

It may show:

(1) A circumscribed or more diffuse infiltration, pneumonic in appearance, varying in extent from a few centimeters in diameter to the involvement of nearly the whole of one lobe of the lung with or without demonstrable tracheobronchial nodes.

(2) A small nodule in the lung with or without visible lymph node masses in the hilum.

(3) Circumscribed masses of caseous nodes projecting outward from the mediastinum.

(4) Masses of calcified tracheobronchial nodes and no obvious lesion of the lung.

(5) Rarely, an area of infiltration with a rarefied center due to excavation and usually associated with enlarged uncalcified tracheobronchial nodes.

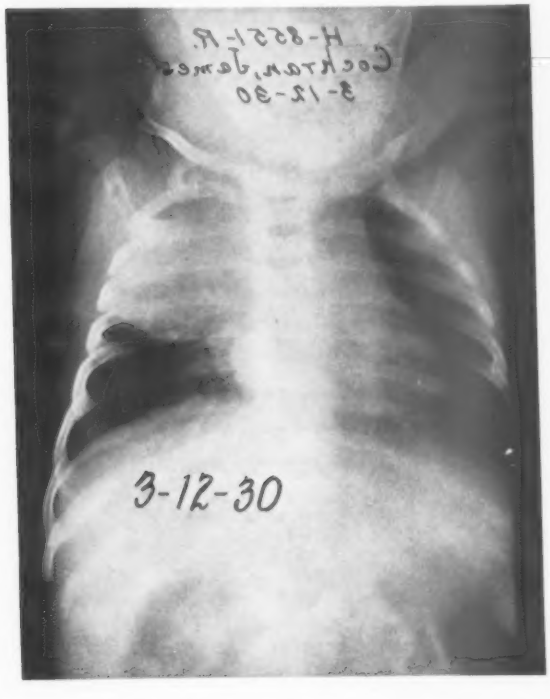

Fig. 1*a*. Colored baby aged four months. Diagnosis: Childhood type of tuberculosis. Massive parenchymatous infiltration right upper and middle lobe with extensive tracheobronchial lymph node involvement. It is not unusual in children under five years of age for the immediate reaction to the presence of tubercle to produce the roentgenological appearance of a pneumonia. The course is chronic instead of acute. It takes months instead of days for resolution to take place. (See Fig. 1*b*.)

Fig. 1*b*. Same child as in Figure 1*a* thirteen months later. Childhood type of tuberculosis showing a regression of disease. Resorption of exudate in parenchyma has taken place slowly. Calcium is being deposited in the caseous center of the primary nodule (Ghon tubercle). The associated lymph nodes show some reduction and decrease in density.

One with a clear concept of the pathogenesis of pulmonary tuberculosis should be able when interpreting roentgenograms of children to visualize the whole picture, to reconstruct the preceding segment of the cycle, and to form an opinion as to the gravity of an existing lesion. With experience this can be done with a reasonable degree of accuracy and satisfaction.

When we find areas of infiltration of the exudative or productive types and associated with them are calcified pulmonary nodules or tracheobronchial nodes, we can conclude that the active lesion is of the adult type of tuberculosis and that it has been superimposed on the childhood type, which has existed for a considerable time. In cases I have observed in white children, it has taken about two years for lesions to become well calcified. In colored children,

FIG. 2. Colored child aged seven years. Diagnosis: Childhood type of tuberculosis. This differs from Figure 1 in that parenchymatous involvement is very slight and the tracheobronchial lymph node involvement is massive. Primary nodule (Ghon tubercle) can be seen opposite left fourth anterior rib. This is becoming calcified. There is a deposit of calcium in the mass of nodes showing in the second left interspace. We rarely see such large tuberculous lymph nodes in white children.

I have seen well marked calcifications develop in one year.

The characteristics of the tuberculous lesions caused by reinfection, or what we now call the adult type of tuberculosis, are usually clear cut and can be demonstrated without difficulty. Occasionally, however, an exudative lesion may present a problem that would baffle the roentgenologist who has only the film for evidence. In such cases, age, history, symptoms, and time for serial films may be necessary to determine the genesis of the lesion.

The roentgenological points to look for are fibrosis, so prominent in adult type and so minimal in childhood type tuberculosis. The presence of associated tracheobronchial lymph nodes and of calcium should be noted. The presence of calcium in parenchymal nodules or tracheobronchial lymph nodes is valid evidence of a preceding tuberculous focus, and any fresh lesion appearing thereafter must be due to a subsequent infection and therefore is the adult type of disease.

There are, however, many cases of adult type of tuberculosis in which there is no evidence of an earlier lesion to be seen in the film. It may have been entirely absorbed or be hidden behind a rib, the dome of the diaphragm or the heart. Then again, the primary infection may have been implanted elsewhere, as in the tonsils, cervical or mesenteric lymph nodes. In these

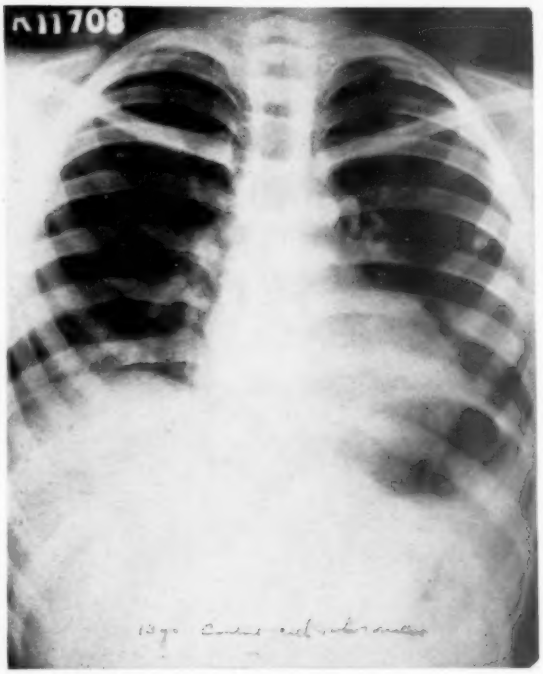

FIG. 3. White boy aged thirteen years. Childhood type tuberculosis illustrating a later phase of the disease. Ranke's primary complex shown in the well-calcified primary nodule in the lung parenchyma opposite third left anterior rib and the calcified tracheobronchial lymph nodes at the left hilum draining this area. Following the implantation of tubercle bacilli in the left lung an exudate formed and slowly absorbed. The center of the tuberculous nodule underwent caseation, and calcium was deposited therein. It usually takes two years or more in white children for a calcium deposit to become as dense as is shown in this film.

extrapulmonary cases a subsequent infection of the lung with tubercle bacilli is followed by the adult type of pulmonary tuberculosis. As this reinfection has taken place in sensitized tissue, the lesion remains localized in the parenchyma, and the tracheobronchial lymph nodes do not become involved. The disease, therefore, manifests the same characteristics regardless of whether the primary infection occurred in the lung or in some other part of the body.

It is of prognostic importance to determine whether a given lesion is the childhood or adult type. In the former, the lesion tends to retrogression. Treatment in many cases requires only general hygiene and the prevention of further infection. The prognosis is good. In the latter, the lesion tends to progress. Treatment must be rest in one or more of its applied forms, and this often means a complete change in the patient's plans for the future. The prognosis is doubtful. Periods of quiescence alternating with re-activation may continue over a long period of time before healing is established even in favorable cases.

Fig. 5*a*. White girl aged fourteen years. Diagnosis: Childhood type of tuberculosis. Calcified primary nodules at third right anterior rib. Numerous calcified areas at the roots of both lungs. No physical signs or symptoms of disease. This represents a healing phase of childhood tuberculosis, but Figure 5*b* shows that such benign-appearing lesions are a source of danger during the period of adolescence. (See Fig. 5*b*.)

Fig. 4. Colored girl aged ten years. Diagnosis: Adult type of pulmonary tuberculosis superimposed on the childhood type of tuberculosis. Childhood type is shown by the enlarged tracheobronchial nodes and calcified areas at the right root. A deposit of calcium that is demonstrable by the roentgen ray will take place in colored children sometimes within one year. The exudate that accompanies a primary infection would have largely disappeared within that time. Therefore, the infiltration at the top of the right lung must be recent and the result of a reinfection, either exogenous or endogenous.

In the interpretation of roentgenograms of children's chests, the roentgenologist should not only describe the tuberculous lesions found but should state his impression that they were of the childhood or adult type.

The bronchopneumonia caused by the tubercle bacillus is identical in appearance with that caused by the pneumococcus. The exudate in the former, however, will take weeks and months to resorb, while the latter usually disappears in one to two

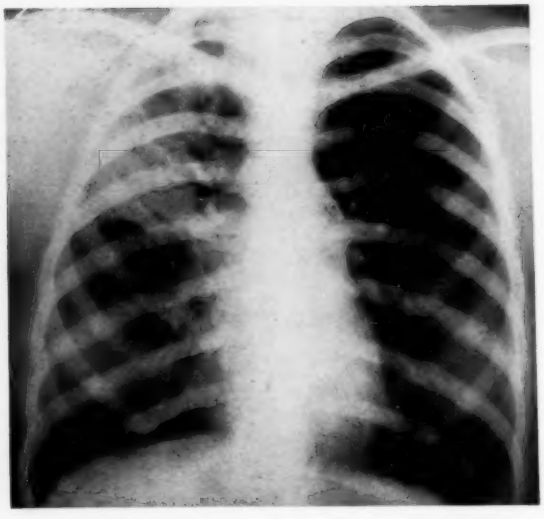

FIG. 5*b*. Same patient as in Figure 5*a* seventeen months later. Diagnosis: Adult type of tuberculosis following the childhood type. While under treatment in a sanatorium the adult type of tuberculosis developed. The reinfection must have been from her own tuberculous foci. Although these appeared in the first film to be well calcified, they or other concealed tuberculous nodes contained tubercle bacilli from which reinfection occurred.

weeks. A roentgenologist often cannot decide which one it is from a single observation. He can only report that it may be either one. The history and symptoms will usually supply the data needed to make the diagnosis, and these may be obtained by the clinician. Other films taken a week or two later will furnish the conclusive evidence. If, however, there are definite uncalcified tracheobronchial nodes with clear cut margins sharply defined by the lung tissue associated with the parenchymal infiltration, then we have confirmatory evidence of its tuberculous origin. This condition is often seen in Negroes, Mexicans and Indians but rarely in white children.

Increased densities at the root of the lung are often due to fibrosis and blood vessels. Calcification occurs in the caseous tissue caused by tuberculosis. It is the signpost marking the trail of the tubercle bacillus. It shows that the invader passed that way. It does not mean that his activities have ceased in that or other locations. Therefore, when we find a deposit of calcium in the lung or lymph node, there is, or has been, a focus of tuberculosis; but we must be certain that it is calcification and not something simulating it.

Blood vessels are often caught in the same axis as the ray, and then they may present a column of blood two or more centimeters in depth, which will produce a density as great as calcium. These vessels are often mistaken for calcified nodes near the root of the lung and along the descending bronchus. These spots are homogeneous in density. They are circular or oval in form with clear cut margins and often accompanied by a bronchus in cross section.

Calcified nodes in contrast are uneven in density, irregular in outline and usually larger in area. Another film taken at a different angle will cause this spot, if made by a blood vessel, to disappear, but if it was due to calcified tissue, it will remain in view. It is a safe rule, when other films can-

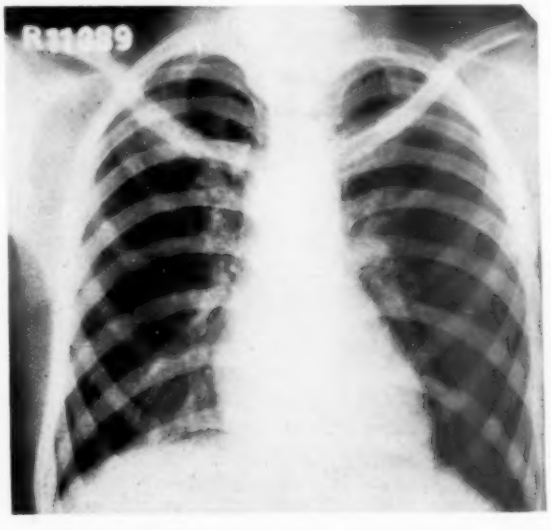

FIG. 6*a*. White boy aged twelve years. Diagnosis: Adult type of tuberculosis. There is a small rounded tuberculous infiltration at right first interspace. At the right root there is a small calcified mass denoting a prior childhood type of tuberculosis. We know that this subapical infiltration is due to a reinfection because of the older lesion of the childhood type at the root. Such lesions are usually progressive and require aggressive treatment. (See Fig. 6*b*.)

not be taken, to class round or oval spots with an even outline and of homogeneous density as blood vessels.

Uncalcified tuberculous nodes are not visible at the root of the lung unless they are large enough to project beyond the margin of the hilum. Then they are clearly outlined by the lung parenchyma, which is of a less density than the caseous nodes. Calcified areas, whether in the parenchymal or in the tracheobronchial nodes, should be reported by the roentgenologist if they are found in a person under twenty years old. Up to that age, it is probable that there are living tubercle bacilli in and about the lesion, and there may be other diseased nodes of more recent origin hidden in the mediastinum. Often, too, calcified and caseous areas coexist in the same node or group of nodes. Calcium is associated with the process of healing a tuberculous focus. We do not know that it promotes healing or makes it more secure. It is not valid evidence that the lesion is healed until adult life is reached. Therefore, a calcifying lesion should be considered a menace throughout childhood.

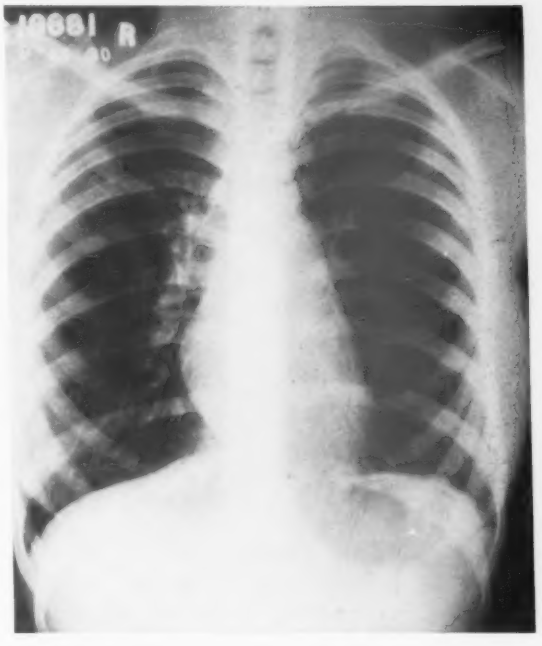

Fig. 7*a*. Colored girl aged sixteen years. Diagnosis: Adult type of tuberculosis. Small infiltration in right second interspace. No evidence of former childhood type of tuberculosis is seen. No physical signs or symptoms. (See Fig. 7*b*.)

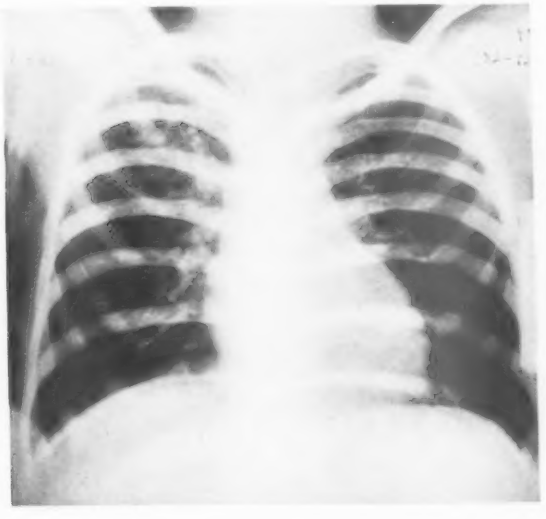

Fig. 6*b*. Same boy one year later. As there were no signs or symptoms of tuberculosis other than the roentgen evidence, the family physician did not consider treatment indicated. The boy continued in school. The film taken after the lapse of one year shows progressive pulmonary tuberculosis now involving the upper third of the right lung.

Rarely, a calcified tuberculous focus in children becomes obsolete. In these cases, the bacilli have died out and the skin sensitiveness to tuberculo-protein has disappeared. More often, however, blood vessels in cross section are mistaken for tuberculous foci. They appear as rounded or oval areas at the root of the lung and along the descending bronchus. Whenever the tuberculin test is negative in such instances, we should seriously question the accuracy of the roentgen interpretation.

I know of no better way to acquire a standard by which to interpret the varied changes that are caused by tuberculosis than to first study the films of many apparently healthy children and then check the interpretations with the tuberculin test. One who does that for the first time will be surprised to see the variations in density at the root of the lung in the films of children

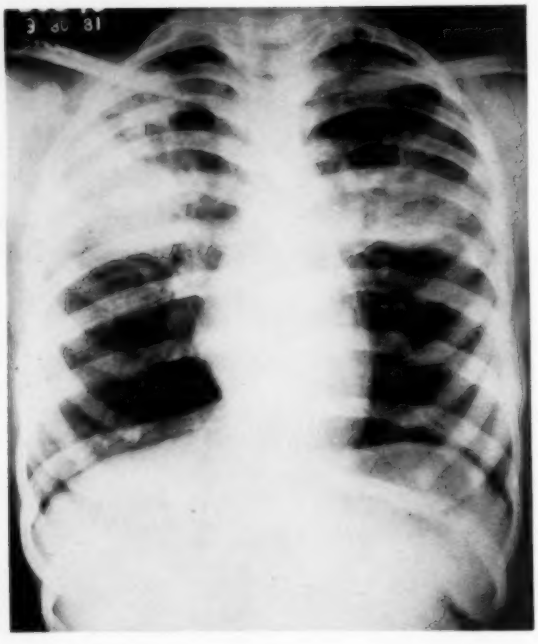

FIG. 7*b*. Same patient as in Figure 7*a* one year later. Infiltration now involves the upper half of the right lung and a large area in the middle third of the left lung. This case and one shown in Figure 6 show how small lesions if of the adult type may rapidly progress. Diagnosis in such cases must be made by the roentgenogram as physical signs or symptoms are rarely present. A routine tuberculin test and roentgen examination of all reactors is the only way to discover these early cases. After a diagnosis of pulmonary tuberculosis of the adult type is made in children and adolescents, pneumothorax or phrenicectomy is the treatment that is most effective in staying the progress of the disease. The prognosis is extremely grave when only routine sanatorium or home treatment is carried out.

who have not even been infected with tuberculosis.

The blood in the larger vessels at the hilum and along the lower poles produces most of the normal densities seen in those regions, and the volume of blood contained in those vessels varies with diastole and systole. The hilum area also changes in width with inspiration and expiration. There may be fibrotic changes that are the residue of former acute infections and of chronic disease of the upper respiratory tract that will broaden and deepen the shadows. Also, variations in technique in taking and developing films will minimize or accentuate these densities. Therefore, one must have all of these factors in mind when viewing films.

We are using sound judgment and are on safe ground when we interpret as tuberculous lesions only those densities in the hilum area that appear as discrete masses containing calcium and such uncalcified nodes as are large enough to project as rounded masses beyond the tissues of similar density normally present at the root of the lung.

In conclusion, I wish to emphasize the significance and importance of the childhood type of tuberculosis, both from the standpoint of the patient and public health. Although usually benign, it is often the ancestor, sometimes quite remote, of the more serious adult type of tuberculosis. We know that the adult type of this disease can develop only in sensitized tissue made so by a preceding infection, and that the lesions caused by that early infection are often the source of the bacilli that produce the pulmonary tuberculosis of later years.

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HEPATOGRAPHY AND LIENOGRAPHY FOLLOWING THE INJECTION OF THORIUM DIOXIDE SOL (THOROTRAST)*

By WILLIAM H. STEWART, M.D., MAX EINHORN, M.D., *and* H. EARL ILLICK, M.D.
NEW YORK CITY

WITH the hope that the liver could be more definitely outlined (hepatography) and also the spleen (lienography), we first used tetraiodophenolphthalein, the results of which investigation have already been reported[1]. Our experience has been that while this drug and method are useful, there is insufficient clarity in the hepatic shadows obtained to demonstrate the finer structural changes. Lately we have been using thorotrast by means of which the liver and spleen may be clearly and sharply outlined. In one case neoplastic formations in the liver could be distinctly seen. We have had opportunity so far to use thorotrast in a series of 8 cases.

MODE OF ADMINISTRATION

Ampules of thorotrast, or thorium dioxide sol, were furnished by the Heyden Company, each of which contained 3 grams of thorium suspended in 12 c.c. of water. The ampule was immersed in a beaker of alcohol for cleansing purposes and contents were then added to 18 c.c. of physiological salt solution and the mixture injected intravenously, very slowly. Another ampule, sometimes one and one-half, would be injected the next day or the day following, depending on the patient's condition and reaction to the first injection.

ROENTGEN FINDINGS

At first, films were exposed every few hours after the first injection but no changes in the density of the liver or spleen could be recognized until at least twenty-four hours following the first injection. The density of the liver and spleen slowly reaches a maximum in about a week or two, depending on the number of injections, and this is then retained as long as any of the patients have been under observation, in our only living case of the series for eight months.

VALUE OF THE TEST

Nearly all of the patients who were examined had enlarged livers as a result of some kind of pathological involvement. In all cases except one, who died too soon to obtain any perceptible increased density, the liver shadow was rendered opaque and the outline was more sharply defined. The patient who received a total of four injections has a liver density about equal to a barium-filled stomach. This is still the same eight months after the test. The best splenic density was obtained in Case VI, in which the hepatic shadow was less dense. In one case (Case IV), the density of the liver was mottled like a leopard; this was diagnosed and later confirmed at autopsy as malignancy.

The value of the test is in clearly outlining the liver and spleen, thus enabling differentiation from other intraabdominal masses. In occasional cases even considerable enlargement of the spleen had not been previously recognized by other clinical methods. Certain malignant involvement of the liver is diagnosable from a characteristic roentgen appearance. Cirrhosis and other generalized hepatic enlargement gave no characteristic findings except to register the increased size.

REACTIONS AND DANGERS OF THE TEST

The material was well tolerated up to an hour after injection in all cases. Five had no definite after-effects. Three had vomiting attacks after the second injection for several days and two patients had hemorrhages. At this date 7 of the 8 cases are dead. However, none of these deaths is

* Read at the Thirty-second Annual Meeting, American Roentgen Ray Society, Atlantic City, N.J., Sept. 22–25, 1931.

FIG. 1.

directly attributable to the thorotrast; all had severe pathology sufficient to easily account for death and not one would have lived, even if the test had not been made.

The thorium dioxide sol is deposited in the endothelial cells of the liver and spleen thus rendering these organs visible. The material is probably permanently present and is at least a potential source of future trouble. In one case at autopsy the spleen left over a photographic plate for a day contained enough thorium to register an image on the plate while control spleens were negative. Four autopsied cases showed acute splenitis. Whether this is due in any way to the thorotrast is questionable.

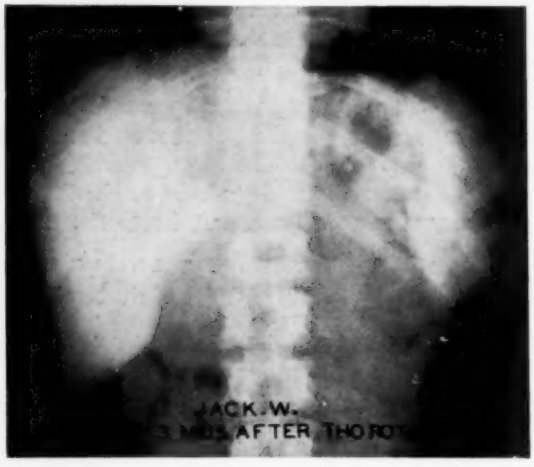

FIG. 2.

In conclusion, the study demonstrates that excellent hepatic and splenic outlines and detail are obtainable following the use of thorotrast intravenously. The thorium is retained indefinitely in the liver and spleen; the injection is sometimes followed by very severe reactions. Except in unusual cases the test does not seem to yield enough independent information to justify its use. Following are brief histories with roentgenograms of 7 of the 8 cases in our series.

SUMMARY OF CASES

CASE 1 (No. 29016). J. W., male, aged forty-two. Admitted Jan. 3, 1931; discharged Feb. 21, 1931.

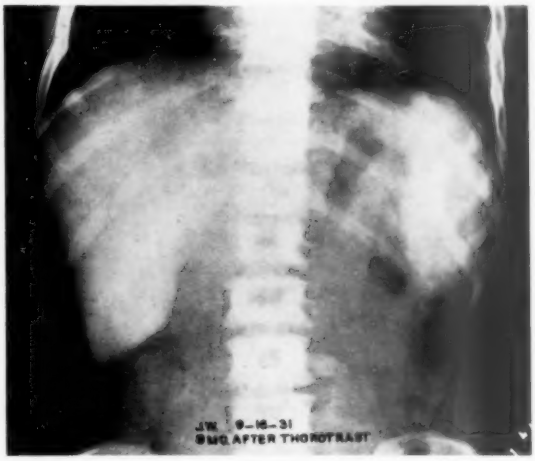

FIG. 3.

The patient had suffered from epigastric pain and vomiting after meals for four weeks, coming on about half an hour after meals and lasting up to two hours; vomiting during last week. On physical examination both liver and spleen were found somewhat enlarged. Roentgen examination showed a poor filling of the duodenal cap but no definite ulcer; the stomach was empty at six hours.

Examination of the blood showed: red blood cells, 9,650,000; hemoglobin, 150 per cent.

Thorotrast (1 ampule) was injected on Jan. 24; 1½ ampules on Jan. 26; 2 ampules on Jan. 28, and 3 ampules on Jan. 30. Roentgen examination showed liver and spleen enlarged, and increased density found to extreme degree up to eight months from the time of injection

when the patient reported; he was then feeling fine, working, and had gained 30 pounds.

Final diagnosis: Polycythemia. (Patient had little if any effect from the injections.) (Figs. 1, 2 and 3.)

Case II (No. 29207). R. S., male, aged fifty-one. Admitted Jan. 20, 1931.

For the past two months the patient has had an average of two watery stools a day without pain; for the past ten days there has been mid-abdominal and epigastric pain coming on about two hours after meals; he then vomits and feels relieved.

Physical examination revealed a slightly enlarged liver; spleen not palpated. Roentgen examination showed a penetrating ulcer on the middle of the lesser curvature about the size of

Fig. 4.

the end of a thumb; stomach empty at six hours.

Thorotrast (1 ampule) was injected on Jan. 30; 1½ ampules on Jan. 31, and 2 ampules on Feb. 2. No immediate or later effects were complained of or elicited on direct questioning. The liver was found enlarged, with increased density; spleen intensified but apparently not enlarged. No metastases recognizable (Fig. 4). The patient was operated on and diagnosis of ulcer confirmed. Death occurred from peritonitis on March 1, 1931. Autopsy limited to findings through operative incision.

Case III (No. 5499). A. H., female, aged sixty-five. Admitted Feb. 3, 1931; discharged Feb. 10, 1931.

The patient had pain, nausea and vomiting

Fig. 5.

for the last six or eight weeks; there is a mass in the epigastrium and a nodular liver. Has lost 22 pounds in the last month; also has difficulty in swallowing; swallowing sound not heard at 22 seconds.

Roentgen examination showed cancer in the pyloric third of the stomach, probably extending up to the cardiac orifice; moderate gastric residue at six hours.

Thorotrast (1 ampule) injected on Feb. 3; 2 ampules on Feb. 5. There was no reaction from the first injection; had vomiting attacks for four days after the second injection; also "weak" spells with rapid pulse. There was no apparent enlargement of the liver; slightly increased density of liver and spleen (Fig. 5).

Fig. 6.

CASE IV (No. 29265). J. S., male, aged forty-nine. Admitted March 21, 1931.

The patient complained of pain in the upper abdomen. On examination the liver was found enlarged and a diagnosis of cirrhosis was made.

FIG. 7.

The Wassermann test was negative. The spleen was just palpable.

Roentgen examination of the stomach and duodenum was negative.

Thorotrast (1 ampule) was injected on Feb. 8; 2 ampules on Feb. 9. There were no reactions of any kind. The liver was found to be huge and mottled like a leopard skin, and became very dense. The spleen was also enlarged and opaque (Figs. 6 and 7). The patient died on April 29.

Autopsy. Liver, weight 4,350 grams. There were numerous, small, raised, greenish nodules from pea to plum size; on section the liver substance was almost entirely replaced by these nodules. On microscopic examination a diagnosis of multiple malignant adenomata was made. The spleen weighed 400 grams and showed changes from acute and chronic splenitis. Sections of the pieces of the spleen were placed in Petri dishes and photographic plates placed over them in a dark room for twenty-four hours. Definite shadows were cast on the plates. The spleen controls were negative. These findings would favor the presence of thorium in the spleen.

CASE V (No. 29032). F. P., male, aged forty-nine. Admitted Jan. 21, 1931.

The patient had suffered from cough, loss of weight, night sweats, occasional blood-tinged sputum, and dyspnea for nearly two years. At times had attacks of chills and fever. Has feeling of substernal and subcostal pressure. Wassermann reaction, four plus.

Roentgen examination of the chest showed what at first was thought to be a lung tumor; but later a diagnosis of tuberculosis was made. There was a much enlarged cardiac shadow.

Thorotrast was given when the possibility of lung tumor was considered, to determine presence of metastases in the liver. One ampule was given on Feb. 17; no reaction. No more was given as the patient seemed too sick. A roentgenogram taken twenty-four hours after the injection shows the liver somewhat increased in density and plainly outlined. The spleen is also enlarged but not dense (Fig. 8).

The patient died on June 15, 1931. Autopsy revealed chronic passive congestion of the liver, weight 2,175 grams; spleen, weight 375 grams, patchy congestion of the pulp on section; microscopically acute and chronic splenitis.

CASE VI (No. 16245). C. L., male, aged seventy-four. Admitted March 12, 1931.

Patient has suffered from lower abdominal pain for three years; gas on stomach for five

FIG. 8.

years; the pain comes on usually at night and lasts for three or four hours. Lately has felt weak and tires easily; moderate loss of weight, 51 pounds in five years.

Physical examination reveals a greatly enlarged liver; spleen just palpable. Icterus; positive Wassermann reaction. A diagnosis of cirrhosis was made.

Thorotrast (1 ampule) was injected on March 19; no immediate reaction; forty-eight hours later complained of slight tenderness over the spleen on direct questioning.

Roentgenograms demonstrated liver enlarged and somewhat dense; spleen moderately enlarged and very dense (Fig. 9).

Patient died from erysipelas on April 9, 1931. Autopsy revealed liver weight 1,225 grams; surface hobnailed; microscopic examination showed marked atrophic cirrhosis; endothelial cells swollen and some show varying stages of necrosis. Spleen, weight 325 grams, pulp soft. Microscopic examination showed the endothelial cells to be swollen and many necrotic. The changes were regarded by the pathologist as explainable on the basis of the acute infection.

Case vii (No. 27436). S. L., male, aged thirty-seven. Admitted March 10, 1931.

The patient complained of jaundice, vomiting, weakness, tender abdomen, and feeling of fullness in the region of the liver. On physical examination the liver was found enlarged three fingers below the costal arch; spleen palpable.

Thorotrast (1 ampule) was injected on April 1; no immediate reaction. Seven hours later the patient spit up half a basin of frothy blood over a period of several hours. Next day he was much better, with smaller mass palpable. Several months later he had another spell, and bleeding at this time was believed to come from gums and esophagus.

Fig. 9.

Fig. 10.

Roentgenograms demonstrated liver enlargement and considerable enlargement of the spleen with increased density (Fig. 10).

On May 1 a cholecystectomy was performed. The patient died on June 13, 1931.

At autopsy the liver weighed 1,675 grams and was deeply jaundiced. Microscopically there was a very extensive cirrhosis of the extra- and intra-acinar types. The cells were degenerated; some areas showed an acute process with necrosis. The spleen showed acute and chronic splenitis.

In the eighth case there was an ulcerating cancer of the stomach. Twelve hours after the thorotrast injection there was a severe gastric hemorrhage.

We wish to express our thanks and appreciation for the assistance rendered by the Pathological Department of the Lenox Hill Hospital.

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DISCUSSION

DR. RICHARD LEWISOHN, New York City. In opening the discussion I would like to say that the few animal experiments I have made and the pictures taken at Mt. Sinai Hospital, have led us to exactly the same conclusions as Dr. Stewart. In other words, it seems to me, one may say we have come here, if not to bury thorotrast, certainly not to praise it. We have 5 clinical cases. The pictures were taken in Dr. Jaches' department at Mt. Sinai Hospital.

My reason for taking part in this discussion is that I have performed some animal experiments with thorotrast. Roentgenograms of these animals and the microscopic sections, which were studied by Dr. Klemperer, may be of interest to this Society. I am in complete agreement with the speaker that the intravenous injection of thorotrast seems to have no immediate ill effect on the patients.

The injections were given to the patients according to Radt's directions. No reaction, either in the form of a rise of temperature or chill, was observed. The patients had a large liver or spleen or enlargement of both organs, as demonstrated by palpation.

In the 5 cases, either liver or spleen or both are fairly well outlined. However, the thorotrast fails to bring out details of structure, for instance, carcinomatous metastases.

Animal experiments were performed on 4 rabbits in April, 1931, according to Radt's directions. In 2 cases the organs were not well outlined; in the other 2, the spleen was demonstrated very clearly on the film.

Microscopic examination of liver and spleen of 2 animals (death five days after injection of the primary dose and a few hours after the injection of a second dose of thorotrast in larger amount) shows the following: The reticulo-endothelial system was filled with deposits of the injected material. Some of the cells showed nuclear damage. In the third case (death three weeks after injection of thorotrast) the nuclear damage was conspicuous, whereas in the fourth animal (death 26 days after injection) some tissue repair was apparent.

Conclusions: The intravenous injection of thorotrast has no immediate ill effect on the patient. It gives an outline of either liver or spleen or both organs without finer details. Its aid in the clinical diagnosis of diseases of the liver and spleen seems to be limited. At present thorotrast cannot be compared in diagnostic efficacy with uroselectan and similar drugs for kidney diseases or lipiodol for lung diseases.

The hope is expressed that some other drug based on a different biological principle will soon be found which will allow an accurate roentgenologic diagnosis of diseases of the liver and spleen.

(Dr. Lewisohn presented slides.)

DR. I. S. RAVDIN, Philadelphia. I think that Dr. Stewart has done a very good deed in bringing before this Society the dangers of this method. If one reads the articles published by Dr. Radt, one cannot help but believe that the dangers of this method are few. Thorotrast is deposited in the reticulo-endothelial system. This system is extremely widespread in the liver, in the spleen, in the vascular system and in the bone marrow.

From the slides shown by Dr. Lewisohn one can see that there is extensive damage to these cells. Neither the physiologist, the anatomist, nor the clinician knows as yet just what the reticulo-endothelial system does in its entirety, but it probably plays an important part in certain processes. In phagocytosis it plays an important part and it probably has something to do with certain types of jaundice. It plays an important part in blood cell regeneration. Therefore, one must look with great hesitancy on using a method which will cause damage, if not destruction, to that system.

About a year and a half ago we began using a mixture of an iodized oil, campiodol with acacia, with a similar idea. It is based upon exactly the same principle. If one injects an iodized oil and acacia intravenously in an experimental animal, one finds after the injection of several ampules that the liver and the spleen begin to be visualized. But here, too, one is introducing a substance which is taken up by the reticulo-endothelial system. The exact extent of the damage cannot be estimated, and for that reason we felt that it was an unsafe measure to go ahead with.

We have had no personal experience with thorotrast and I have been intensely interested in hearing these two unfavorable contributions of American investigators who have had the opportunity of using it.

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THE NICHE IN THE DIAGNOSIS OF JEJUNAL ULCER

By JACOB BUCKSTEIN, M.D.
NEW YORK CITY

IT WAS Reiche[25] who in 1909, put the roentgen diagnosis of ulcer upon a firm and sound foundation. He had occasion to examine by means of the roentgen ray, a patient aged forty-seven, with a history of serious gastric disturbance of several years' duration. He noticed in the roentgenogram, the stomach filled with bismuth and in the middle of the lesser curvature a small, mushroom-shaped protuberance. The patient died of hemorrhage. At autopsy, an ulcer of the lesser curvature was found, round, about the size of a quarter, deeply penetrating and with smooth margins, and corresponding in position to the pouch in the roentgen picture. A practical method of diagnosis of chronic gastric ulcer was thus definitely established.

Haudek[17] in 1910 elaborated upon and popularized the roentgen method in the diagnosis of ulcer. He verified its practical value in numerous cases that were proved to be correct by surgery or autopsy, and demonstrated the importance of the niche as the only absolute diagnostic criterion. The contributions of Reiche and Haudek received recognition in the work of Faulhaber[16] and Holzknecht[19] and soon became universally accepted as a solid basis for the diagnosis of gastric ulcer.

Similar significance regarding the diagnostic value of the niche in duodenal ulcer was eventually established through the work of Barclay,[4] Haudek,[18] Bier,[8] Kreuzfuchs,[20] Rieder,[26] Strauss,[28] Cole,[15] Case,[13] Buckstein,[9] and more particularly through the contributions of Åkerlund,[1] Berg,[6,7] and Albrecht.[2]

That the niche corresponding to the crater of a jejunal ulcer may be demonstrable with clearness, and with equivalent diagnostic value, has not been so completely realized.

Bársony[5] was apparently the first to demonstrate the roentgenographic appearance of a niche as evidence of a gastrojejunal ulcer.

Zollschan[30] reported 3 cases in which he felt that a diagnosis of peptic ulcer of the jejunum was justified, with operative proof in one case. In all three, a gastroenterostomy had been performed, with the development sometime later of new symptoms accompanied by occult hemorrhages. On roentgenographic examination he found a residual area of barium in the efferent jejunum painful to localized pressure. One of the cases was operated on, and the tender, niche-like area containing a barium residue was found to correspond to the crater of a jejunal ulcer. As the appearance in the other two non-operated cases was similar, he believed that here too he was dealing with roentgen evidence of an ulcer niche.

Ström[29] reported his experience following the examination of 300 patients after operation for ulcer and concluded that it was possible to demonstrate niche formation at the site of anastomosis as characteristic of ulcer, similar in diagnostic value to the finding of a niche in gastric or duodenal ulcer.

Owing to the normally irregular appearance of the jejunum due to the valvulae conniventes, the demonstration of such niche formation is much more difficult. This difficulty is increased if the involved area in the jejunum is overlapped by the barium-filled lower pole of the stomach. In the technical demonstration of such niche formation, Ström emphasizes the following points: (1) the importance of properly applied pressure to the area under observation; (2) giving the patient a second opaque meal several hours after the first to demonstrate the relation of any niche-like area to the course of the gastrojejunal anastomosis; (3) the value of several roentgenograms to show the persistence of the defect.

Palugyay[24] summarizes his observations by reiterating the value of the niche, or the presence of a gastrocolic or jejunocolic fistula as the direct criteria in the diagnosis of peptic ulcer of the jejunum.

FIG. 1.

In the examination of the stoma following gastroenterostomy, Case[14] recommends visualization through every angle, and occasionally in the Trendelenburg position. In patients who are well after a satisfactory gastroenterostomy, the form of the stomach is normal, no irregularities or filling defects are present due to the operation, the emptying time is from one to five hours and the passage of the barium through the stoma is generally rhythmic.

The most reliable sign of gastrojejunal ulcer in his opinion is evidence of an ulcer crater, but this is only rarely seen. More commonly the diagnosis depends on deformity at the site of the stoma, fixation and localized tenderness.

Moore and Marquis[23] reviewed 200 cases of gastrojejunal ulcer at the Mayo Clinic in the preceding ten years. The lesion had developed as early as six weeks after operation in one case, and twenty-one years later in another. The most common type is penetrating in character and while usually situated in the suture line, may be at some distance from the stoma, in one case being 9 cm. away.

In roentgenologic demonstration of the direct evidence of jejunal ulcer, the importance of palpation is emphasized, the separation of the overhanging stomach from the small intestine and a careful inspection for evidence of deformity with rotation of the patient through varying degrees of obliquity. The presence of craters should be looked for carefully, but the authors consider such findings as infrequent and believe that barium retained within the folds of the jejunum has been erroneously interpreted as the niche of a true crater.

Carman[11,12] stated that, with the exception of one case, he had not noted any roentgenological evidence of a cavity resembling the niche of penetrating gastric ulcer or the accessory pocket of perforating ulcer. The nature of the ulcer rather precludes any probability of visualizing its crater as a niche, for the reason that the ulcer is most often characterized by considerable surface extent rather than depth.

However, Carman in a review of presumably the same material at the Mayo

FIG. 2.

Clinic as used by Moore and Marquis, wrote with more definiteness of the value of the niche as direct evidence of a jejunal ulcer. Following a gastroenterostomy with normal function of the stoma, the stomach is usually smaller, peristalsis may be diminished, and the duodenum is not dilated. The barium passes through the stoma continuously or intermittently into the jejunum, which retains its normal size, and regularity of contour.

Of the indirect signs of ulcer, the following findings may be present: gastric enlargement, six-hour retention, hyperperistalsis and duodenal dilatation. None of these, however, is conclusive. He refers also to deformity and narrowing of the stoma and of the efferent jejunal loop. However, only the niche is absolutely pathognomonic, as the other factors may be produced by other causes such as traction from a short efferent loop or adhesions, or from herniation of the jejunum through the opening in the gastrocolic mesentery. Two beautiful examples are included, one a roentgenogram showing a perforated jejunal ulcer which produced an accessory pocket, and another, a typical niche just beyond the stoma.

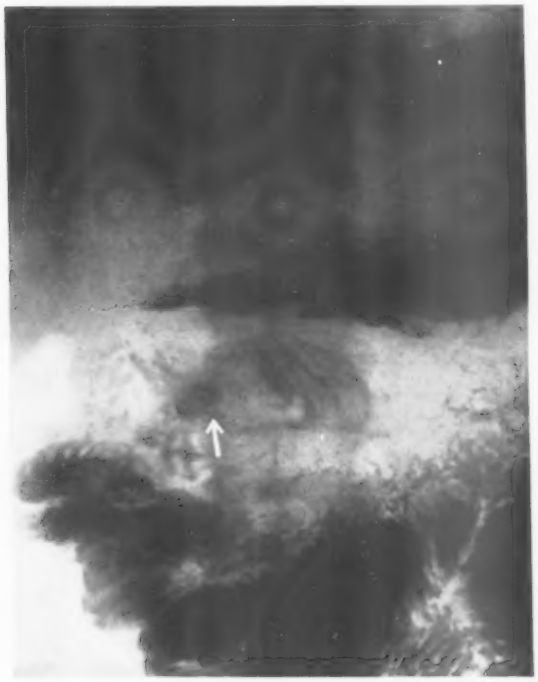

Fig. 3.

Scott[27] recorded three roentgenograms showing characteristic niche formation in jejunal ulcer and described his technique of "white-washing" the gastrojejunal area with a small amount of a barium-cream mixture, by means of palpation behind the fluoroscopic screen, and carefully searching for retention of the barium within a crater.

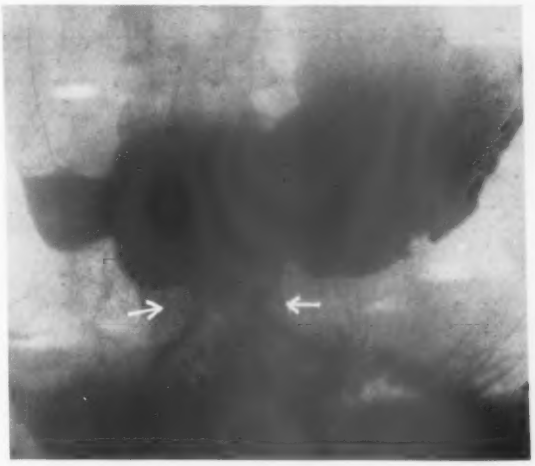

Fig. 4.

Lindqvist[21] in 1926 reported a case that was examined in 1923, with a roentgen diagnosis of a peptic ulcer of the jejunum penetrating into the anterior abdominal wall. A giant niche was visible in the roentgenogram just distal to the stoma. This he confirmed at operation. The roentgenogram demonstrating the niche accompanies the article.

Allen[3] recorded the case of a man who developed a marginal ulcer following a gastroenterostomy for duodenal ulcer. He was operated on and a partial gastrectomy performed. He again developed a marginal ulcer with a typical niche, as noted in the accompanying roentgenogram. This was verified at a third operation at which the marginal ulcer was resected. Another typical niche of a jejunal ulcer was noted in a case with surgical confirmation.

Camp[10] emphasized the significance of the niche in the diagnosis of peptic ulcer of

the jejunum as the most reliable criterion, and recorded many excellent examples from his large experience.

The importance of graded compression in the demonstration of the niche of jejunal

FIG. 5. Jejunal ulcer with niche formation.

ulcer, has been particularly studied by Berg,[7] Albrecht[2] and Meyer-Burgdorff and Schmidt.[22]

In addition to the niche itself, they have thereby been able to show the radiation of the folds of mucous membrane in relation to it.

Clear roentgenologic evidence of the niche as a diagnostic criterion in jejunal ulcer is indicated in the accompanying case reports.

CONCLUSIONS

1. A historical survey is presented of the value of the niche in the roentgen diagnosis of gastric and duodenal ulcer.

2. Similar diagnostic value may be placed upon the demonstration of the niche in the diagnosis of jejunal ulcer.

CASE REPORTS

CASE I. S. A., aged fifty-two, had been operated on one year previously for an ulcer of the first portion of the duodenum, and a gastroenterostomy was performed. He remained well for four months. Intermittent epigastric pain developed which grew steadily more severe. The pain was relieved by food for one hour and then recurred. It might last all night. No vomiting was present.

Physical examination revealed tenderness at a point just above the umbilicus in the midline.

At operation a small ulcer was found, involving the jejunum just beyond the stomach. The ulcer was beginning to perforate into the mesentery and was also becoming adherent to the transverse colon. A partial gastrectomy was done.

In the accompanying roentgenogram (Fig. 1) the arrow points to a persistent niche formation. In addition there is marked dilatation of the beginning of the jejunum in that region, with narrowing just beyond the niche. The stoma showed diminution of mobility. Tenderness was localized to the site of the niche. No six-hour retention of the motor meal was noted.

The patient later developed evidence of obstruction at the site of the new enterostomy, with gastric retention at twenty-four hours.

CASE II. F. M., aged twenty-four, had been suffering for six months with periodic recurrences of epigastric pain, relieved by food. The pain then returned several hours later. It would occasionally awaken him at night. No vomiting or tarry stools were present. A duodenal ulcer

FIG. 6. Jejunal ulcer with niche formation. Note also radiating folds of mucous membrane associated with niche.

was found roentgenologically and at operation. A gastroenterostomy was performed. For ten weeks he felt relieved. A gnawing distress in the upper abdomen then developed, occurring one-half to one hour after meals, which was relieved by food.

Five months later he was re-operated on. An area of induration just distal to the lower end of the stoma was found. The colon was fixed to the jejunum at this site. The colon was separated. There was a perforation extending partly through its wall, without involving the mucosa. The gastroenterostomy stoma was separated. An ulcer of the jejunum was excised. The duodenal ulcer was still present and apparently showed no signs of having healed. A partial gastrectomy was performed. The patient developed bronchopneumonia and died.

The significant points in the roentgen diagnosis of the jejunal ulcer were these: (1) irregularity of the stoma with niche formation, as indicated by the arrow in Figure 2; (2) localized acute tenderness at that site; (3) diminution of mobility; (4) a six-hour retention of the motor meal, limited to the site of the stoma.

Case III. P. C., aged twenty-three, had a history of periodic recurrences of abdominal distress, for which he sought surgical relief. He was operated on elsewhere, five months prior to admission to the hospital. A gastroenterostomy was performed for duodenal ulcer. He was well for one month, when he began to suffer intermittent pain located in the right upper quadrant. The pain was boring in character, at times knife-like, and was relieved by food. The pain might awaken him from sleep at night.

Fig. 7. Jejunal ulcer with niche formation.

Fig. 8. Niche of jejunal ulcer showing radiating folds of mucosa.

Physical examination showed slight voluntary rigidity of the right rectus muscle, and tenderness in the right upper quadrant.

Roentgenographic examination revealed the presence of a niche on the jejunal side of the stoma, with localized tenderness and fixation. The niche is indicated by the arrow in the accompanying roentgenogram (Fig. 3).

At operation, considerable inflammatory reaction was present around the stoma and a large ulcer was found. A gastric resection was performed.

Case IV. P. J., aged forty-four, had been operated on one month previously for an ulcer, 1 inch in diameter, involving the lesser curvature of the pars media. On re-admission to the hospital, he complained of constant vomiting and diarrhea. No blood was present in the vomitus or in the stools. He had lost considerable flesh and strength.

On physical examination, the scar of the former operative procedure was noted. Tenderness was present in the epigastrium. Peristalsis could be observed through the thin abdominal wall.

At operation, there were numerous adhesions at the site of the gastroenterostomy. A jejunal ulcer was present, which had perforated through into the colon.

On roentgenographic examination the stoma appeared irregular with niche formation (Fig. 4). There was marked diminution of mobility, and tenderness was localized at the site of anastomosis. A diagnosis of marginal ulcer was made. Communication between the stoma and the colon, which was suspected because of the history of diarrhea, could not be demonstrated roentgenographically by means of the ingested meal. Examination following a barium enema was therefore suggested, as this will more frequently and clearly show the presence of a gastrocolic fistula. Operation, however, was decided upon before examination could be made.

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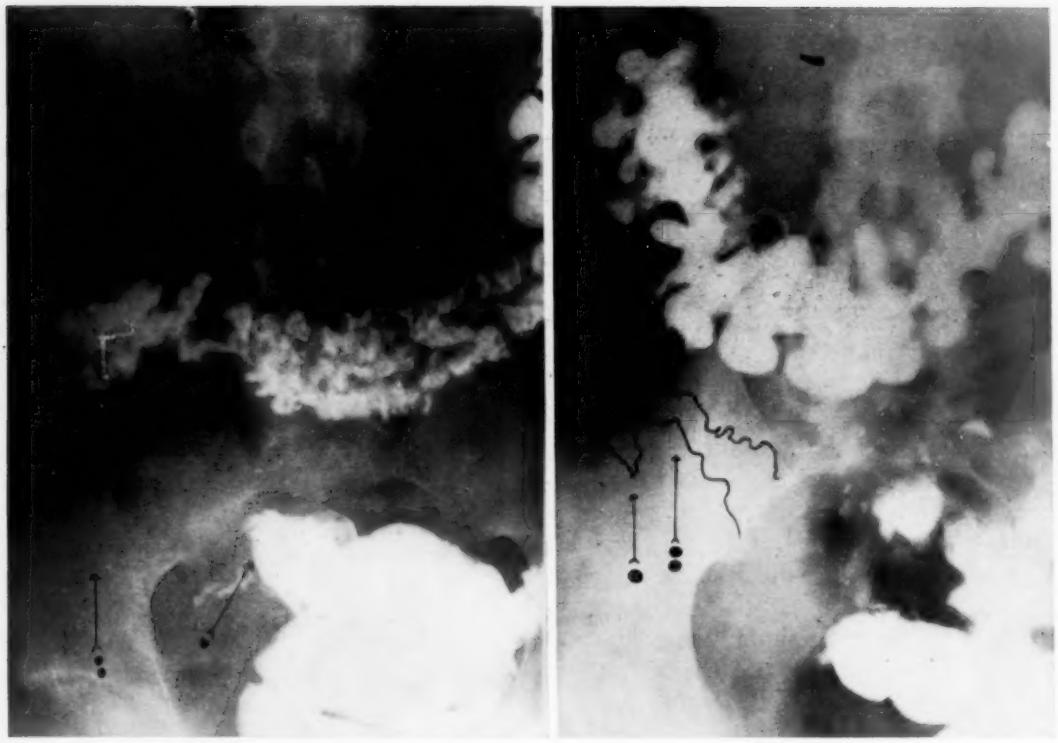
SIGNS OF TUBERCULOUS ENTEROCOLITIS

By HOMER H. CHERRY, M.D.
Waverley Hills Sanatorium
WAVERLEY HILLS, KENTUCKY

STIERLIN[38] in 1911 published what he thought to be roentgen-ray signs of intestinal tuberculosis. He corroborated his contentions with a series of seven autopsies; Kienböck did likewise in 1913 and demonstrated at autopsy that he was correct in each instance; Archibald[1] reported on a series of cases in 1917. The work of these observers acted as an impetus to many others and from time to time roentgenologists have found themselves especially interested in this phase of diagnosis. Brown and Sampson[5] published a series of cases in 1919 describing the early symptomatic and roentgen signs; again in 1922 they[6] published a series of 39 cases, 38 of which were corroborated at surgical exploration; their monograph[7] on the subject followed in 1926, giving a most comprehensive idea of the complication. With the advent in more recent years of therapeutic measures aimed at, and in many instances successfully, healing the more favorable cases, it becomes additionally imperative that everyone concerned with the treatment of tuberculosis know definitely if their cases have intestinal complications. There are roentgenologic and clinical changes occurring along with healing of the ulcerous tract that are reliable, and are moderate assurance of the patient's recovery. Consequently we have reasons why cases should be examined for this complication at intervals during the course of treatment. The earlier workers directed their attention at finding the so-called Stierlin's sign.[38] When the distal ileum was found dilated with opaque medium, the cecum and proximal ascending colon empty and more distal parts of the colon well filled (Fig. 1), they knew that disease existed in the region of the cecum and that it was defeating the physiological purpose of this portion of the tract, which is to act as a reservoir. Their efforts very nearly ceased here, chiefly on account of a consorted assertion that the whole procedure held out little hope of securing reliable information in a substantial number of cases. They all

FIG. 1. An extreme type of spasm resulting from tuberculous ulceration in the region of the cecum is here illustrated. Arrow one points to the cecum which is almost obliterated. Arrow two illustrates a segment of small intestine which has ulceration proximal and distal.

felt that if Stierlin's sign was present it was reliable, but they thought its absence did not exclude the possibility of disease and that the authenticity of the method for any other part of the tract could not be substantiated. Such men as Schwarz and Novascinsky[35] maintained that the streaky and marble-like appearance (Fig. 2*a*) described by Stierlin[39] was unreliable. His sign in the opinion of Faulhaber[17,18] and Chanol[13] may be absent in many cases. Brinsmade[11] more recently found old and



(*a*) (*b*)

FIG. 2. (*a*) This is an illustration of the marble-like appearance described by Stierlin. Arrow one points to a segment of small intestine. Arrow two points to the region of the cecum. This structure is completely empty. (*b*) For the twenty-four hour motility to indicate ulceration requires no more than that the cecum and proximal ascending colon be empty, but this must show no trace of barium. In this illustration the eight-hour film has been superimposed on the twenty-four hour film and the outline of the cecum and ascending colon indicated by ink outline. Arrow one indicates the cecum; arrow two indicates the end of the ileum.

healed ulcers at autopsy without there having been any clinical or roentgenologic evidence. Steinbach[40] insists, along with others,[7,25,32] that the absence of all signs does not exclude the possibility of extensive lesions. I wish to share their opinions but not with the same acquiescence. Steinbach concluded that the whole procedure was unreliable. It is found, however, that the average length of time between roentgen examination and autopsy of this series was fifty-one days longer for the disagreeing group than for the agreeing group. This is important and probably accounts for much of the variation in opinion on the subject. He intimates, and with this I strongly disagree, that intestinal tuberculosis "is usually a terminal phenomenon." Gatellifr, Moutier and Porcher,[22] and Fenwick and Dodwell[19] express opinions similar to this. Williams,[41] although not discouraged at the value of the procedure, found only 17 per cent positive ante mortem of a group of cases that disclosed an 80 per cent incident rate post mortem. When we investigate Brown and Sampson's work, more pleasant reading is encountered and the conclusion from their statistics is encouraging.

Regard, however, should be had for the work of all observers and it is agreed that the obstacles are great and that uncertainty arises on every hand.[16] Yet, in line with the present-day need and the accessibility of adequate equipment, it is indicated that a more exhaustive study be made of the whole tract to determine the extent and

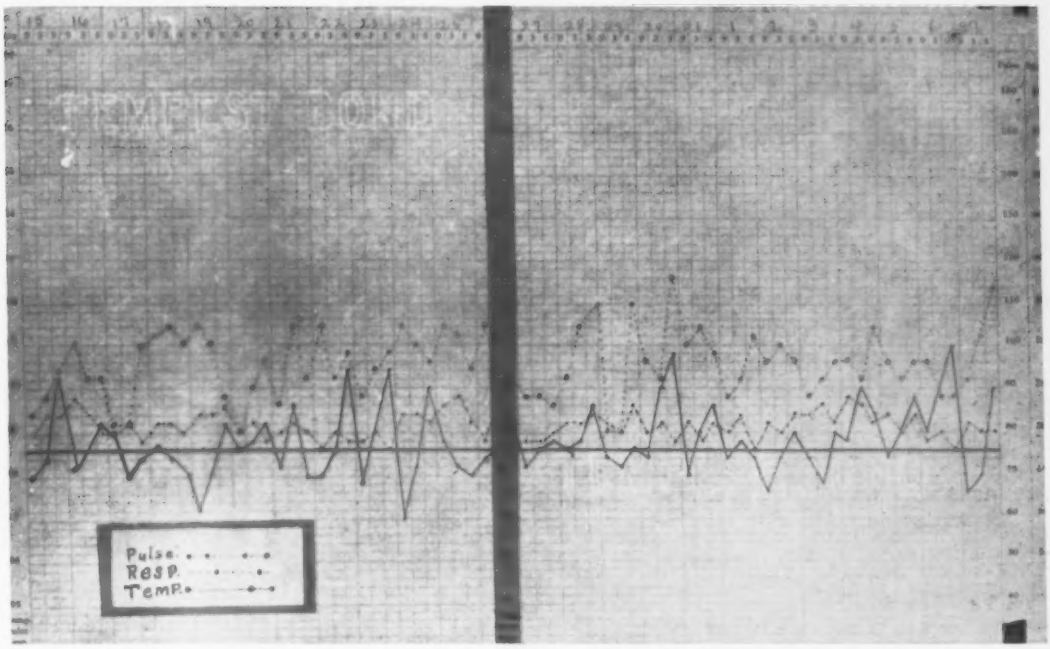


Fig. 3. Chart showing the pulse, temperature and respiration record of a patient suffering from severe colitis.

location of lesions and to arrive at a differentiation of certain pathologic conditions and roentgenologic similarities.

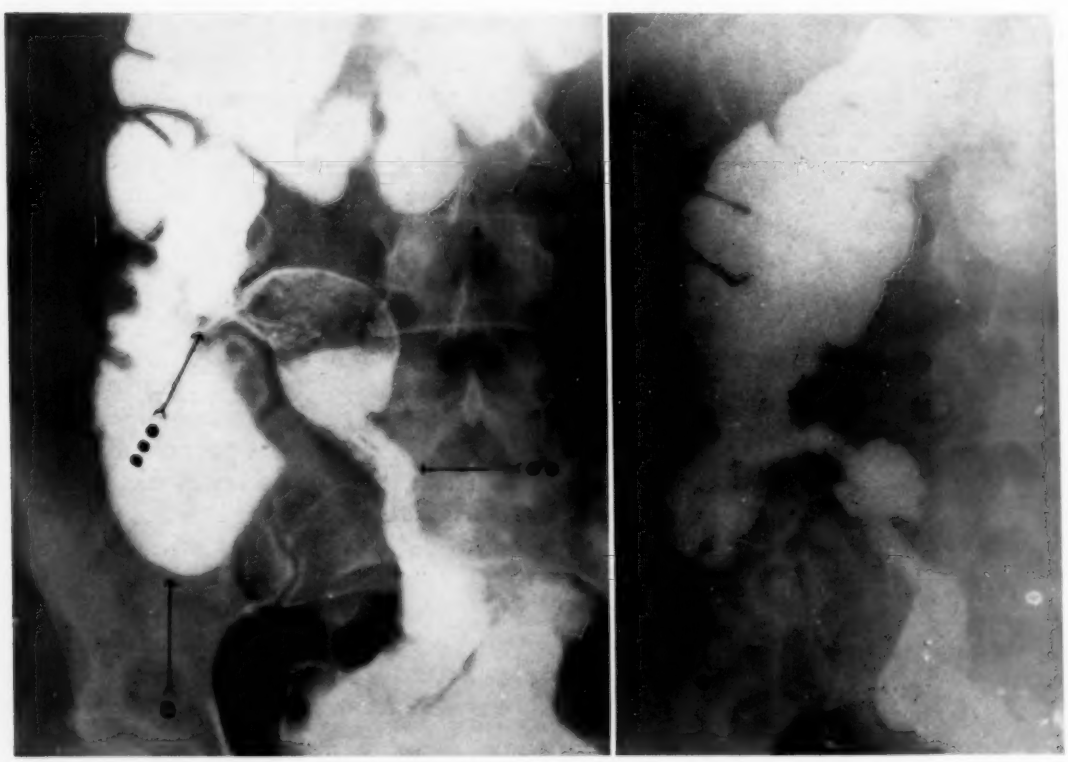
CLINICAL SIGNS

Along with the advance in accurate interpretation of roentgenologic signs has not come a consorted interest in symptomatic and physical manifestations. To me it seems just as essential for the roentgenologist to have the clinical aspects when developing an opinion on a case as it is for the clinician to have the roentgen evidence when his opinion is reached.

There is a tendency to consider too many abdominal symptoms as having a tuberculous origin. Williams listed ten; Brown and Sampson[5] eight. Jordan and Kiefer[28] observed that one-half of the patients coming to their clinic complaining of digestive disturbances were found to have no other pathology than a functional disorder of the colon. Smithies, Weisman and Fremmel[36] found it difficult to prove patients suffering with mild dyspepsia positive roentgenologically for ulceration. Any patient suffering from active pulmonary tuberculosis is apt to complain of eructation, discomfort after meals, and constipation, the latter especially on confinement to bed. Webb and Ryder[42] found constipation usually due to faulty diet and lack of regular habits. Constipation resulting from intestinal tuberculosis is rare and only comes with the onset of adynamic ileus which may be due to severe and diffuse ulceration of the tract and is a reflection of irritated peritoneum instead of intestinal tuberculosis. Inspection of these ulcers at post mortem will reveal that they have approached the subserous layer and that tubercles can be seen beneath the overlying peritoneum. Products of inflammation will also be deposited on the surface of the peritoneum at the site. Two such cases occurred in this series. It is conceded that occasionally an isolated ulcer or even moderately extensive ulceration may exist without symptoms, but a large majority of positive cases[36] will give one or more of the following symptoms: Pain, sharp and not well localized, occurring at night or during the day and some-

times worse after meals is the most common symptom. Celsus[33] said seventeen centuries ago that "paine in the belly . . . trouble those who are very thin." This pain may become so severe that the patient will have great discomfort. The appendix has in these instances become tuberculous. Complete relief of this type of pain was secured in one of our cases by appendectomy, although there was extensive ulceration at other sites along the colon and small intestine; another was found at autopsy to have a large and fibrotic appendix, the lumen of which was dilated with greenish pus; another was found to have a similar condition when pelvic laparotomy was performed.

Profuse diarrhea is unusual; loose stools are the rule; mucus, pus and blood are not to be expected.[16] On the other hand, the stool does not appear abnormal except in an occasional case when it may be watery. Due to putrefaction the odor is foul.[7,32] Alternating periods of loose stools and normal motility are seen. When there is a persistent and severe diarrhea the tubercle bacillus cannot be incriminated.[40] Nausea and vomiting may well be inquired about but they alone are of no significance. Vomiting very frequently is produced by hard coughing and secretions in the posterior pharynx. Nervousness occurring by spells and usually accompanied by increase in temperature (Fig. 3) or loose stools are of significance. Of the objective signs we have only four that are reliable: a cyclic temperature is suggestive (Fig. 3); tenderness on deep palpation over the diseased areas; a palpable mass usually in the right lower quadrant, and mild localized or generalized abdominal rigidity may be found.



(*a*) (*b*)

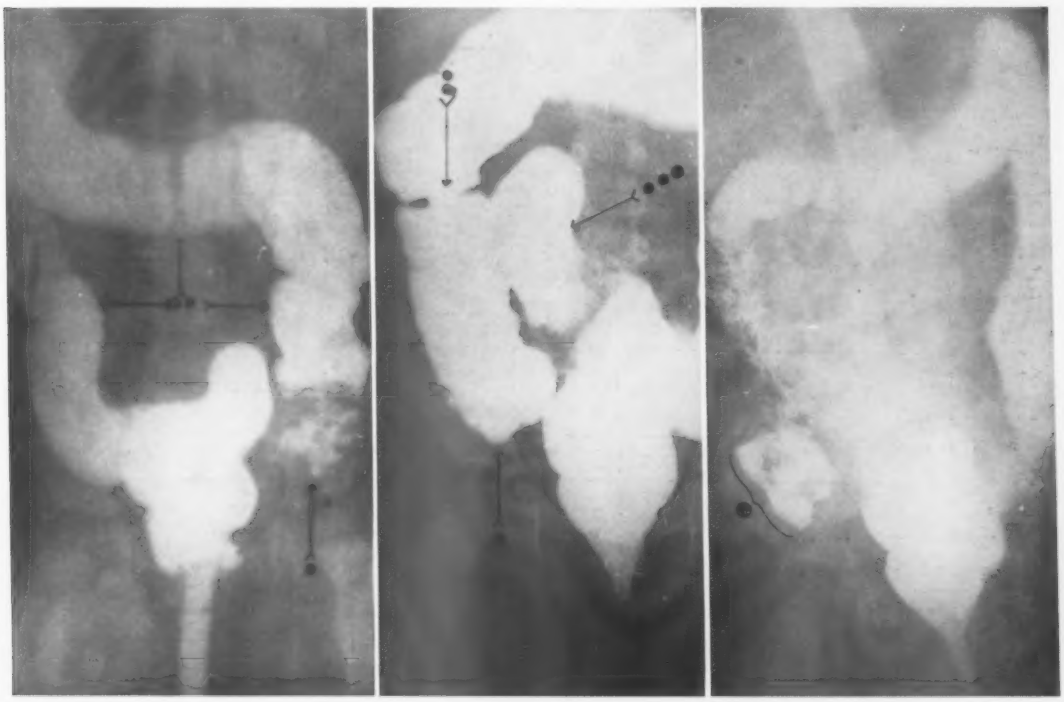
FIG. 4. Arrow one (*a*) points out a normally filling cecum; compare with (*b*) and notice how contracted the cecum has become on being stimulated by gentle palpation. Arrow two (*a*) indicates normal small intestinal contraction. Arrow three indicates Fleischner's sign.

ROENTGEN-RAY SIGNS

For roentgen examination the commonly accepted technique has been used in all of this series. One has the choice of using either the opaque enema or motile meal. The latter is the more reliable[8]; however, it is best to use both methods in conjunction, letting one be a check on the other.

Motile Meal. It is of course necessary to be able to distinguish between all the benign and pathologic distortions, filling defects and variations in motility. In general, it can be said that the motile meal is required for the small intestine and proximal colon.

Turning first to the small intestine we are confronted with the most difficult problem of diagnosis and our conclusion should be based on the presence or absence of pain as described above, persistent segmentation, and nausea accompanied by vomiting. At the distal end of these segmentation loops there is moderate dilatation with pointing. Here, it is difficult to induce the barium to move onwards, and when a forward movement is obtained the intestine immediately ahead seems much contracted (Fig. 1) and the barium is, in a way, spit through. One may be frequently misled when trying to interpret these signs of ulceration of the small intestine. Disease in the end of the ileum may be indicated by marked irritability when manipulated and by persistent contraction with irregular ileal margins. Steinbach reported 4 cases with cecal signs resulting from ulcers in the



(*a*) (*b*) (*c*)

FIG. 5. (*a*) Ulceration is conclusively demonstrated here in the cecum (arrow one). The entire colon is ahaustral and on screen examination irritability was prominent. (*b*) About ten months later the patient had recovered symptomatically and as can be seen the roentgenogram shows a normal colon except for the ahaustral appearance which still persists. Arrow one indicates the cecum; arrow two indicates contraction comparable to a cecocolic sphincter spasm—this is a common site to find it; arrow three indicates the sigmoid colon. (*c*) When the examination illustrated in (*b*) was being made, frequent mass movements were seen to form. All of these took origin at the cecocolic sphincter as seen in the illustration. Bracket one indicates the cecum normally dilated while the colon ahead is in a state of tonic spasm. Observe the fibrillar appearance present.

TABLE I

SUMMARY OF CASES. ONE HUNDRED AND TEN CASES POSITIVE FOR TUBERCULOUS ULCERATION HAVE BEEN REVIEWED

| | | |

end of the ileum. Two such cases occurred in this series. Also the cecum may be thrown into a state of spasm by this manipulation, the signs extending ahead of the diseased segment. If at seven and eight hours the cecum is positive and at twenty-four hours is well filled—providing the twenty-four observation is not made at a time when food particles are present on the mucosa of the terminal ileum—disease in this segment of the bowel is indicated. If the end of the ileum is dilated and there is ileac stasis for more than eight hours, disease in the region of the cecum exists. Fleischner's sign[20] (Fig. 4) should be suspected as existing, especially if the end of the ileum is pointed as it enters the valve. However, we should remember that carcinoma and polyposis can produce a similar roentgen picture.

For signs in the colon it can be generally said that hypermotility,[22] persistent localized intolerance to barium producing filling defects,[7,20] and increase of intolerance on manipulation are the bulwarks for the defense of the procedure. This is in most instances referring to the proximal one-half of the colon; it is here that signs are reflected from ulceration of this segment proper or most commonly the ileocecal region,[23,29] and it is in the ileocecal region that tuberculous ulceration occurs with a preponderant frequency.[4,5,19,30]

Motility. Much can be said concerning the normal motility of the intestinal tract. Kantor,[29] Brown and Sampson,[7] Williams,[41] and others, found that the proximal colon should begin to fill or be filled to the hepatic flexure at six hours; at nine hours the head of the column should be at the splenic flexure and all barium in the colon. There seems to be a diversity of opinion on the twenty-four hour stage. Kantor thinks the proximal colon can normally be empty and that forty-eight hours are usually required for it to become completely empty. Case[12] is of the opinion that it should empty much sooner. It would seem that confusion has resulted from external influence and not as a result of erroneous opinion. Case was working with patients not under the influence of bowel sedatives as codeine so widely

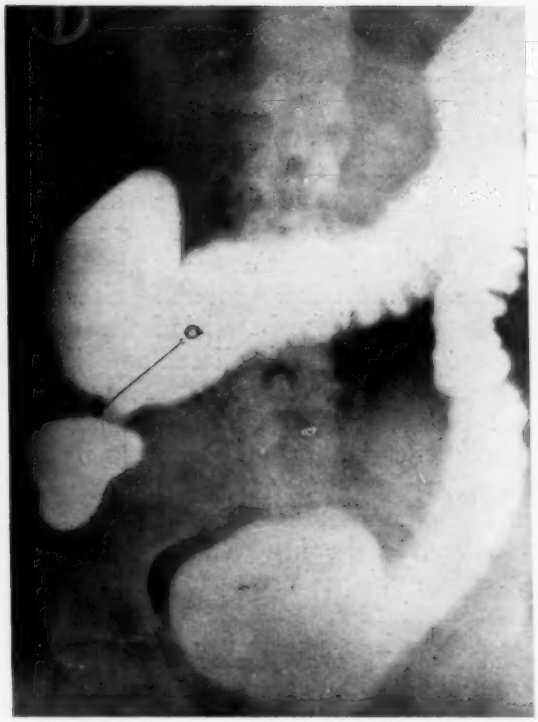
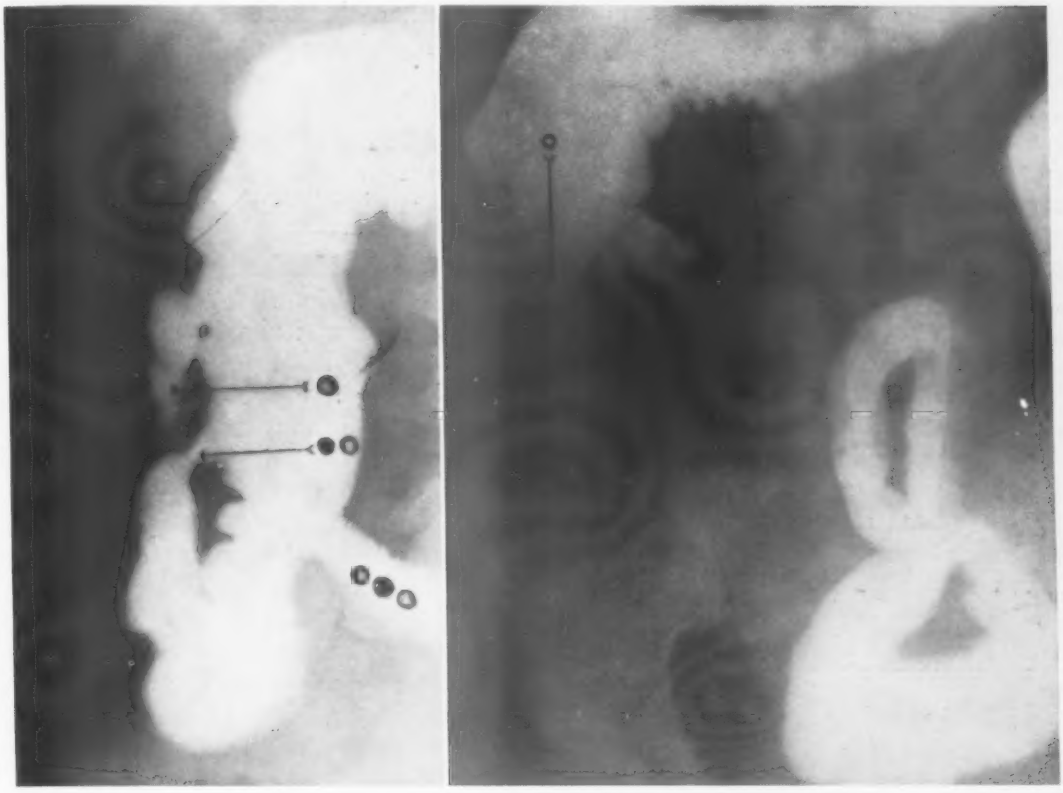


FIG. 6. Illustrating a cecocolic sphincter contraction at its normal position. A mass movement is here in process of early formation.

FIG. 7. Barium flakes surrounded by gas in the proximal colon are often indicative of tuberculous colitis.

used in tuberculosis sanatoriums. Others have worked on general hospital patients which should give the best indices. A large percentage of this group was receiving codeine which undoubtedly slows motility. It can be seen from Table 1 that for the proximal colon to be empty at twenty-four hours is unusual. When it is normally empty the haustra should be well seen and scattered clumps of barium present. If complete emptying (Fig. 2*b*) of the proximal one-half or all of the ascending colon including the cecum exists, disease should be suspected, and it would seem that Stierlin[38] stressed excessively complete emptying of the whole colon. The six- and nine-hour distribution as given seems to be undisputed. At twenty-four hours the barium may normally have any distribution in the distal two-thirds of the colon. There is usually considerable localization of barium and distortion of outline. The areas giving evidence of ulceration at eight and nine hours are usually free of barium at twenty-four hours.

There is likely to be a general shifting of the bowel contents while the screen examination is going on. The barium seems to hasten along into the cecum, quickly through the proximal colon and onwards, the head of the column descending through the distal colon at frequent intervals. This movement in the colon does not simulate the normal mass movement (Fig. 5*c*). Barium pushed into areas of spasm is likely to move freely along. This is the so-called localized hypermotility and is of great significance. Irritability and increase in the size of filling defects on gentle palpation of the ulcerous section accompanies this localized hypermotility.[7,20] When this phenomenon is present in the ileocecal region, tuberculous ulceration should be considered present until proved otherwise[5] (Fig.



(*a*) (*b*)

Fig. 8. (*a*) Arrow one indicates the cecum which is inverted and lies lateral to the ascending colon. Here is illustrated the type of central filling described. Observe the ahaustral appearance and the fine fibrillar margins. Compare this with (*b*). Arrows two and three indicate the distal end of the ileum. (*b*) Arrow one indicates the blunt type of filling encountered in the normal colon. Arrow two indicates a haustrum just beginning to be filled. Arrow three indicates a section of the colon which is characteristic of the so-called fibrillating colon. Observe the notched haustra which are unusually small. This condition is not pathologic.

4). Filling defects resulting from ulceration are almost certain to be persistent on hourly observations and on repetition of the meal.[7,22] When these filling defects occur in the cecum or the ascending colon, they are of great significance; in the transverse colon they are of less significance; in the descending colon and sigmoid of no significance at all unless corroborated by enema. The cecocolic sphincter (Fig. 6) should not be confused with true filling defects. When there is a persistent filling defect in the distal two-thirds of the colon with obliteration of haustra and with irritability on manipulation, one may be led to suspect ulceration. These are the lesions that necessitate the use of the enema.

Less significance should be attached to other roentgen signs given for ulceration of the colon. Barium flakes when located in the proximal colon and surrounded by gas[29,38] (Fig. 7) are strongly suggestive of disease. These flakes represent inflammatory secretions impregnated with barium. A general distribution of gas probably only indicates fermentation. Deep tenderness, when real, may be considered. The marble-like appearance does occur (Fig. 2*a*) but it also occurs in nonulcerative disturbances.[35] Palpation of a mass in the right lower quadrant during the course of examination means that the intestinal serosa has been reached and that a chronic appendicial abscess exists which is of grave concern. This

Fig. 9. The ahaustral appearance of severe mucous colitis is present here. Observe, however, that the entire colon, including the cecum, retains barium well. Compare this illustration with Figure 13 which is a seven-hour observation on the same patient.

did not occur in 1,200 examinations. Generalized and sometimes right-sided abdominal rigidity exists. This occurred in the more acute cases and was usually mild.

The Enema. I would not stress the use of the opaque enema. Its use is confined entirely to the colon where it is moderately reliable (Fig. 9). For the proximal colon it has not the accuracy of the motile meal.[8] Very seldom, if ever, will it be positive for this segment when the motile meal is negative or suggestive. However, it is usually positive when the meal is conclusively positive.

A good technique to follow consists of giving one ounce of magma magnesiae on the evening before the examination. This is done to take away all fecal material so there will be no artificial interference to the column of barium as it moves up the colon. I have always found that the tuberculous colon admits barium with greater reluctance than the normal organ, and at the site of pathology the filling is abruptly checked and is incomplete at first even though subsequently the area becomes normally filled (Fig. 8*a*). If fecal masses lie along the tract, especially if cecal stasis exists, confusion is likely to occur. To have the colon empty at the time of examination is of vital significance and I have no fear of stressing it unduly.

Breakfast is withheld and the patient is taken to the laboratory in the morning, after having had the colon well cleansed with a saline enema, providing free elimination has not resulted from the laxative. The opaque medium should be warm and thin enough to flow freely. Any of the standard preparations on the market today are acceptable. The colon should be filled slowly and with the patient in the supine position. Care should be used not to produce a high pressure.[29] If there has been considerable cicatrization or hyperplasia even with high pressure the areas will remain fairly ahaustral and contracted. Hyperplastic and fi-

Fig. 10. Arrow one indicates marked and persistent spasm of the cecum due to cecal tuberculosis.

brous changes are not the cause of all contraction and ahaustration since at autopsy the colon is found relaxed and normal in size, whereas ante-mortem contraction and obliteration of haustra were pronounced. It would seem to me that a sustained mass peristalsis could account for many of these extreme types of deformity commonly contributed to hyperplasia (Fig. 8*a*). The fine fibrillation seen in mass peristalsis (Fig. 5*c*) is present in many when the enema is being used which attests to this opinion. The ahaustral appearance should not be confused with mucous colitis, which may give a similar picture (Fig. 9). After the areas have been filled, palpation of the site may reveal irritability and increased intolerance to barium if ulceration is present. Anastalsis is not frequently seen; at least this has been my observation, it having occurred in only 4 or 5 cases, some of which were not considered positive for ulceration. Occasionally the barium may be expelled (Fig. 10) promptly from the ulcer area. Here one

Fig. 11. Arrow one indicates a sclerosed and permanently contracted cecum due to hyperplastic cecal tuberculosis resulting in valvular incompetency.

Fig. 12. The string sign in mucous colitis.

may be confused with the beginning of a mass peristalsis (Fig. 5*c*) which seems to have a strong tendency to originate at the cecocolic sphincter (Fig. 5*c*) if that portion of the bowel is full. However, the expulsion of barium due to ulceration is more apt to remain so expelled and confined to the diseased segment (Fig. 10), whereas a mass peristalsis if observed long enough may extend throughout the colon. Frequent formation of normal mass movements may be prompted by minor ulceration. This is unusual. In the region of the ascending colon the cecocolic sphincter[9] (Fig. 6) may offer confusion. Gatellifr, Moutier and Porcher[22] pointed out that filling defects to be of any significance must be present in both prone and upright positions. I wish to share their opinions. It is common to find the barium evacuated in part or all from the ascending colon and especially the hepatic flexure when the patient is observed in a standing position, whereas before arising the same segments were normally filled. This seems to be a siphoning effect produced by the transverse colon prolapsing into the pelvis.

FIG. 13. Seven-hour observation of a case of mucous colitis.

There are certain so-called fibrillating colons (Fig. 8*b*) that should not be confused with pathological ones. Tuberculous colitis ordinarily does not produce obstructive signs in the colon unless there is localized peritonitis with adhesions so that the lumen is encroached upon. Branch's[10] 8 cases with obstructive signs all had hyperplastic lesions of long standing so that as a result of the healing process the lumen had been encroached upon. Since obstruction is uncommon and other signs of malignancy are fairly clear cut, new growths along the tract should offer few difficulties of differentiation. Occasionally during examination by opaque meal as well as by enema, irregularities of filling will be encountered which are due to fecal masses. When these are pushed along the lumen to permit the opaque medium to come in contact with the bowel wall at the site the filling defects vanish and do not reappear. This is especially true for the cecum.

Gershon-Cohen, in his recent résumé on the advantages of the double contrast enema, views with enthusiasm the regularity with which incompetence of the ileocecal valve is associated with early ileocecal tuberculosis. In view of the fact that most workers report that incompetence of the valve is normal in 80 to 90 per cent of cases it would seem hazardous to consider it a

TABLE II

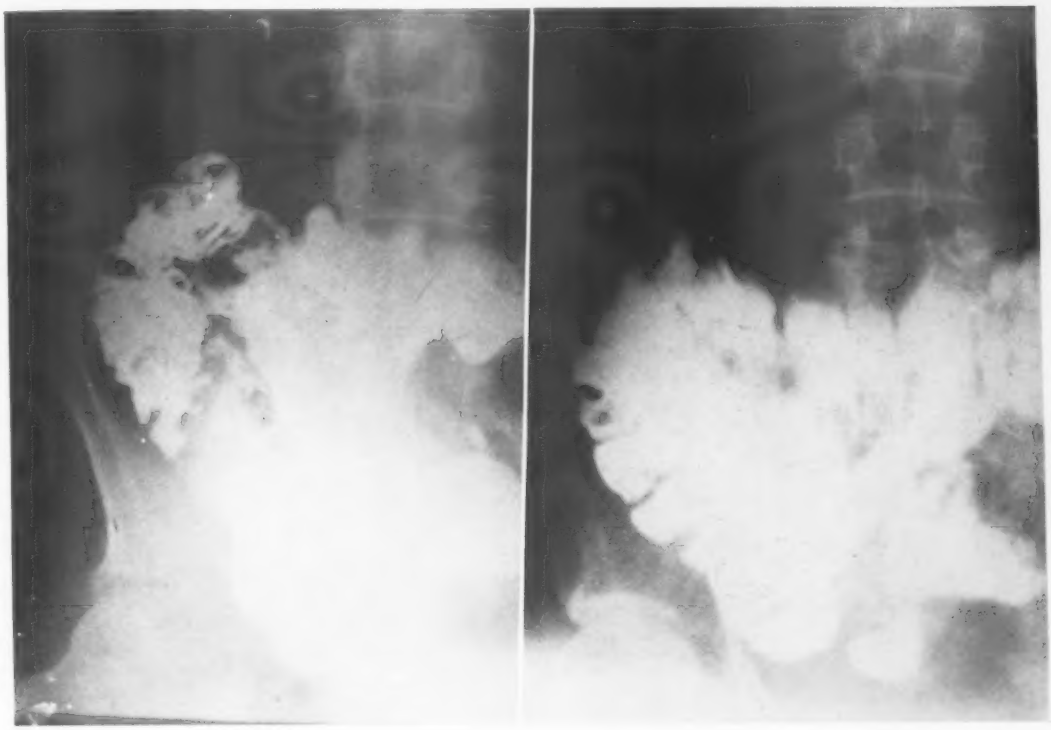
COMPARATIVE ACCURACY OF THE OPAQUE ENEMA AND MOTILE MEAL

Positive meal; Negative enema	Positive enema; meal negative	Meal more conclusively positive than enema	Enema more conclusively positive than meal
12	0	18	3

In 7 patients one method was no more conclusively accurate than the other.

Forty cases that had been examined by both the meal and enema techniques were reviewed to determine the accuracy of the two methods. The greater accuracy of the motile meal should be partly contributed to instances in which the cecum and proximal colon appear positive when in reality the ulceration is in the last few inches of the ileum.

FIG. 14. Healed colon contracted. Compare with Figure 1 which is a roentgenogram of the same case about one year before.



(*a*) (*b*)

Fig. 15. (*a*) Ileocecal tuberculosis before treatment. (*b*) Same case one year later. The twenty-four hour motility was normal.

positive sign except by those of pronounced skill. I would consider the ileocecal valve to be a sphincter capable of functioning as an entity which it does as shown in the formation of Fleischner's sign. This sign is the result of blocking of the barium by spasm of the ileocecal valve and the frenulum valvulae coli and is associated almost constantly with a spastic cecum. Also a study of the genesis of intestinal tuberculosis would indicate that it is futile to interpret incompetence as a sign of early ileocecal tuberculosis. Goldberg, Sweany and Brown[23] and Baldwin, Petroff and Gardner[2] showed that the earliest ulcers usually develop in the last few inches of the ileum or on the valve proper, so it is seen that the incompetence has occurred before the ulcers are reached by the medium. A type of cecum does exist which may inaugurate valve incompetence. It is the indurated and permanently contracted cecum which has resulted in marked and permanent distortion of the valve (Fig. 11). It is easily recognized. As for the double contrast technique[24] I am hopeful. Not all colonic spasms resulting from nerve-end stimulation in ulcer craters are sufficiently strong to resist or expel barium in solution, which has considerable inertia. Air, it seems, would respond most readily to a feeble spasm, and the method used according to the technique of Gershon-Cohen may offer many advantages.

DIFFERENTIATION

Some points of differential significance have been given, but at this time more should be said concerning the separation of tuberculous from nontuberculous lesions.

Mucous colitis is probably most frequently confused with tuberculous ulceration. Crane[15] observed that nervousness,

FIG. 16. Barium enema of a patient with both cecal tuberculosis and mucous colitis. Compare with Figure 18 which is a motile meal examination of the same patient. Observe the ahaustral appearance of the ascending colon and the contracted cecum.

pain, mucous stools and the string sign (Fig. 12) on the second day of observation were the most common signs of mucous colitis. He was convinced that the string sign did not occur in ulceration. This has been observed to be almost constantly true in this series. One case in this series had signs of mucous colitis, on roentgen examination, in the distal half of the colon and tuberculous ulceration in the proximal segment (Fig. 18). Osler thought pain was a prominent symptom. Cawadias[14] divided the clinical syndrome into two diseases. Mucous colitis, he thought, was due to local irritation while spasmomyxorrhea might simulate the former but had as its causes nervousness, reflex pain and systemic intoxication. It is enough to accept these authors' descriptions of the symptomatology of the disease and keep in mind a few constant roentgen signs of differential importance. Schwarz described the colon as more narrow than normal and said that there were frequent changes in areas of apparent filling defects. These are constant findings. Mucous colitis is a distal colitis but it may become so extensive that the entire colon is distorted (Fig. 13); thus one should be led to suspect that ulceration is not present when the entire colon is distorted and especially when the patient has symptoms of mucous disease. Irritability to palpation is far more prominent when ulceration is present. I have come to the conclusion, and am borne out by Hodges,[26] that rigidity, diminution in size and the

FIG. 17. This is a seven-hour film of a motile meal examination of a patient with a spastic colon. Observe the carrot-shaped arrangement of barium which is somewhat characteristic of this type of colon. Patients having a spastic colon are usually middle aged, apprehensive, nervous, and suffer from indigestion. A spastic colon differs from mucous colitis in that the patient never has diarrhea. When the enema is given the haustra appear normally outlined. An enema was required in this instance to determine if tuberculous ulceration was present (Fig. 11). The haustra filled throughout normally; the cecum was found to be sclerosed and permanently contracted due to an old hyperplastic process.

string sign are the constant roentgenologic signs of mucous colitis. The opaque enema reveals the colon to be contracted and ahaustral but not to the same extent as found in chronic nonspecific ulceration.

As far back as 1875 Wilks and Moxon recognized a chronic nonspecific ulceration of the colon. Bassler[3] pointed out that there may be "chronic progressive ulceration of the whole colon" during the course of an infection in which a streptococcus was constantly incriminated. Others[11,31,34,37] have recognized this organism as being the offending agent. Logan,[31] following extensive research intended at determining the etiology of this disease, gave to us the best description of it. Attacks of bloody diarrhea are the chief manifestations. Brinsmade found that it could be present for many years without symptoms. Either an acute or chronic onset is possible.[21,31,34,37] Bassler found the colon to be markedly thickened and distorted and that it most frequently attacked the distal colon and cecum but that any portion and even the small intestine might be involved. For a differentiation of this disease from tuberculous ulceration the following can be kept in mind. When the attack is acute and blood and pus occur in the stool[3,21] and when ulceration is demonstrated in the distal colon by enema, nontuberculous ulceration should be suspected. There is no age limit. The chest should always be examined since primary clinical intestinal tuberculosis probably does not occur.[40] The clinical aspect of this form of colitis can be had from the following case report:

Fig. 19. The enema is less reliable than the motile meal. Compare this negative examination with the conclusively positive motile meal (Fig. 20).

Fig. 18. Ileocecal tuberculosis and mucous colitis are represented here occurring in the same individual.

M. C., white, female child, aged two, was admitted to the ward with the following complaint. During the previous five months the patient had suffered from severe attacks of acute diarrhea, accompanied by vomiting, high temperature and pulse and mild prostration. Considerable bright red blood and pus had occurred in the stools. These attacks would last only two or three days, after which complete recovery would take place. Examination for the different strains of *Bacillus dysenteriae* always proved negative.

Family history was negative except for the mother who had advanced pulmonary tuberculosis.

The physical examination was negative.

Roentgenograms of the chest were negative.

Guinea pigs inoculated with the stool were negative for the tubercle bacillus.

Progress. The patient showed no indication of digestive disorders or other forms of disease for a number of days after admission. Stools appeared normal. She then had an attack which simulated very closely those of which history had been secured. The temperature rose rapidly to 104° F; pulse became rapid; respirations rapid; there were mild symptoms of shock; the stools were frequent, thin and composed chiefly of pus and bright red blood. For the first twenty-four hours vomiting was frequent.

FIG. 20. Seven-hour observation of a motile meal examination revealing cecal tuberculosis. Observe the markedly dilated terminal ileum (arrow one).

Treatment was instituted and at the end of five days complete recovery had apparently taken place. A barium enema was then given the patient, and ulceration was conclusively demonstrated in the region of the cecum and ascending colon. The descending colon also filled slowly, dilating with considerable reluctance and showing some irritability. The haustra were much less prominent than normal (Fig. 5*a*).

The patient had two similar attacks within the following few weeks. For the past six months she has been free of symptoms. The enema examination at the present time shows much less evidence of ulceration (Fig. 5*b*).

Of course, it is necessary to demonstrate in all cases of colitis with blood and pus that the *Endamoeba histolytica*, *Bacillus dysenteriae* and possibly the *Endamoeba coli* are not present.

THE HEALED COLON

I, too, shall not advance any criteria by which we may assert with absolute confidence ante mortem that tuberculous ulceration has completely healed. It is true that healing is observed post mortem and at operation. Brown and Sampson,[9] Goldberg, Sweany and Brown, Baldwin, Petroff and Gardner, Williams, Holden, Branch, Opie, and others, have demonstrated this, and we are encouraged by these observations to describe signs ante mortem that suggest a healed state. At least it is interesting to observe the changing picture as healing goes on. In general, we can say that all the signs of ulceration are replaced by those of a normal colon with the following exceptions. The diseased segment most usually becomes less pliable, indicating healing by cicatrization, and it is usually diminished in size[10] (Fig. 14), yet it may regain a normal pliability, contour, mobility and size (Fig. 15*b*). Although a common finding in progressive intestinal disease, adhesions between the ascending and prolapsed transverse segments of the colon may occur when healing takes place. This is not a good sign since it indicates that an extensive and destructive process has existed. Reference to the work of Baldwin and his associates reveals that the diseased segment may become dilated as a result of destruction without regeneration of the muscularis, in which instance scar tissue made up of inelastic fibers develops. I have not seen dilatation occur. The important observation to make is that it has reëstab-

lished normal tolerance to barium and until this finding is constant over a period of two to three years one should hold out little hope that complete healing has taken place. As Goldberg, Sweany and Brown observed, they seem to wax and wane with considerable irregularity. It seems almost essential that the chest improve correspondingly, although Brown and Sampson,[9] who reported 24 per cent of 360 cases recovering, found extensive healing of ulcerous tracts in 5 cases dying of pulmonary disease. I have never seen a report of complete healing of all ulcers in the presence of progressive and fatal pulmonary disease. I have observed spontaneous recovery from severe colitis following successful pneumothorax therapy. First to go are the clinical manifestations. These may disappear and the roentgen signs remain stationary. These are usually the patients whose chests are not doing well, and in these instances the patient may report that all of his symptoms have disappeared, including loose stools, but the twenty-four hour motility will be increased at roentgen examination, corroborating the seven-and eight-hour signs of an ulcerated colon.

CONCLUSIONS

1. Although the accurate diagnosis of intestinal tuberculosis varies with increasing irregularity as segments more remote from the ileocecal region in either direction are studied, the procedure merits concerted effort. If there are intestinal lesions one or more are sure to occur in the ileocecal region. Also symptoms occur much more frequently than commonly believed, so that when roentgen and subjective signs are carefully considered a large percentage of positive cases are detected.

2. Constipation is rarely a sign of intestinal tuberculosis. Pain and loose stools are the most constant symptoms.

3. The opaque meal is of more value than the opaque enema and is the only method of accurately interpreting the progress of a case.

4. There are no definite criteria by which we may conclude that ulceration has completely healed. There are signs of improvement which are moderate proof, when present from two to three years, the patient having no tubercle bacilli in his sputum for the same period, that healing has probably occurred.

5. The twenty-four hour motility is of great significance when trying to diagnose ulceration. No more than the ascending colon may be empty but this should be entirely destitute of barium. Any segment of the colon having ulceration is usually entirely free of barium at the twenty-four hour examination.

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ROENTGEN-RAY PELVIMETRY—A SIMPLIFIED STEREO-ROENTGENOGRAPHIC METHOD*

By PAUL C. HODGES, Ph.D., M.D. *and* ALFRED C. LEDOUX, M.D.
CHICAGO, ILLINOIS

AS LONG ago as 1897 methods were devised to compute the obstetrical diameters of the human pelvis by calculations based on measurements of roentgen-ray shadows. Hirsch[19] has classified published methods into five groups: (1) comparative, (2) teleroentgenographic, (3) frame methods, (4) simple triangulation and (5) stereoscopic triangulation. We prefer to recognize only two major groups which we designate (1) position methods and (2) parallax methods. Our paper deals with the relative merits of these two groups and describes a particular parallax method developed in our own laboratory.

POSITION METHODS

Hirsch's groups 1, 2 and 3 have one common feature—they all involve the arrangement of the patient in relation to the film as an essential step.

In the comparative method a supposedly normal dried pelvis is arranged in a particular position relative to the roentgen film and the ratios of actual skeletal measurements to roentgen shadow measurements are computed. These ratios are then applied to the roentgenograms obtained by roentgenographing living subjects arranged in the same position.

In the teleroentgenographic method the distortion due to divergence of radiation is reduced to an insignificant amount by the well-recognized procedure of using a long target-film distance; but positioning of the patient relative to the film is essential in order to avoid the distortion that ensues if the planes of the object and film are not parallel.

Fabre[13,14,15,16] and Thoms[42–49] have popularized the frame method and, modified in one way or another, it is in fairly active use today. Thoms' method differs slightly from that of Fabre but illustrates the principle employed by both. The patient is placed on the roentgen table in the semi-recumbent position and the distance is measured from pubic symphysis to film and from just above the spinous process of the fifth lumbar vertebra to film. Anatomically these two points are in the plane of the inlet, so if they can be located accurately one can establish the relative positions of inlet and film. After the film has been exposed and the patient removed from the table, but with tube and film undisturbed, a lead plate perforated at intervals of 1 cm. is arranged above the table in the supposed plane of the pelvic inlet and a second exposure is made.

The holes in the lead plate show in the finished film as black dots slightly more than 1 cm. apart where the plate was close to the film and still further separated where the plate was farther away. Assuming that the lead marker lay in the plane of the pelvic inlet, the examiner reads off the diameters of the inlet directly from the film using these dots as a scale rule.

Walton[53,54] has recently published a graph which he uses instead of the perforated lead plate of Thoms. The patient is positioned with the plane of the pelvic inlet parallel to the plane of the film and at a known distance from its surface. The roentgen tube is centered over the center of the inlet at a target-film distance of exactly 30 inches. On the completed film caliper measurements are made of any inlet diameter. The caliper is placed on the graph at a distance above the base line equal to the supposed distance between pelvic inlet and film and the true diameter is read off directly. Walton's scale has been

* From the Division of Roentgenology, Department of Medicine, University of Chicago, Ill. Read at the Thirty-second Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 22-25, 1931.

prepared by actually photographing a test object at various elevations above the film and recording the distortion that occurs. It

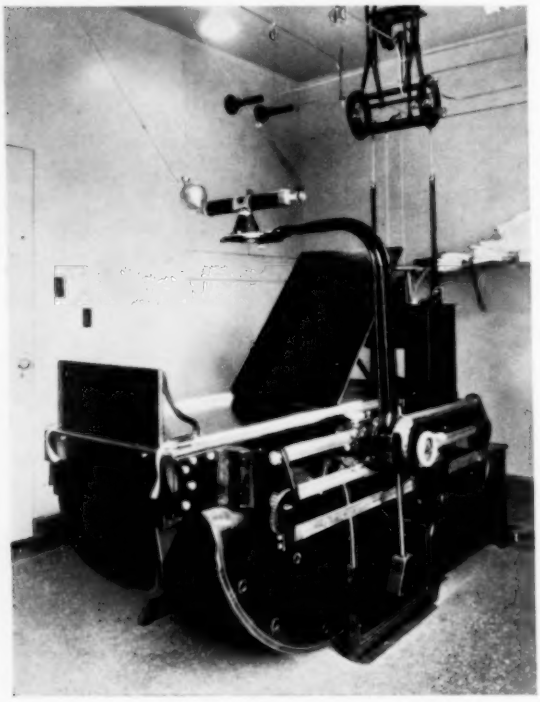


FIG. 1. An obstetrical roentgen table.* The table provides for all ordinary roentgenoscopy or filming in horizontal, vertical and intermediate positions and in addition allows stereoscopic triangulation with accurately fixed target-film distance and tube shift. Angular position of the back-rest is adjustable and the rest is prevented from sliding backward by means of adjustable straps. Registration of the films is accomplished by a marker attached to the tray of the Potter grid.

is, of course, perfectly feasible to compute the graph from the equation

$$\frac{O}{X} = \frac{D-Y}{D} \text{ where}$$

O = the actual diameter of the object.
X = the diameter of the roentgen shadow of the object.
D = the target-film distance.
Y = the object-film distance.

Proponents of the position methods consider them simple and reasonably accurate. In the sense that few special devices or mathematical computations are required they are simple. On the other hand, the person making the film must be qualified to examine the patient, locate certain anatomical landmarks accurately and then exert considerable care in positioning patient and apparatus.

Accuracy cannot be checked as easily as one might suppose. Roentgenographing a dried pelvis does not suffice because it is a simple matter to identify the plane of the pelvic inlet in the dried pelvis but difficult to do so in the living subject.

There is the further objection that, at best, these methods furnish accurate quantitative information at only one plane through the pelvis.

Experience may show that the position methods are sufficiently accurate for clinical purposes and perhaps they will continue to be most easily available and, therefore, most popular for routine obstetrical work. On the other hand, there appears to be need for modern tables of obstetrical diameters and for this purpose as well as to serve as a check on the position methods a more precise and less subjective method is needed.

PARALLAX METHODS

In all of the position methods it is necessary to establish by physical examination the distance between the planes of object and film, together with the angular relationship between these planes. In the parallax methods these relationships are computed from measurements of roentgen shadows, target-film distance and roentgen tube shift. Position methods, therefore, involve practically all of the inaccuracies of parallax methods plus whatever inaccuracy may be inherent in the physical examination of the patient.

SIMPLE TRIANGULATION

The underlying principles of the parallax methods have a very wide application in astronomy, navigation, gun-sighting, surveying, etc. Their application to roentgenology in the past has been largely in

* Developed for use at the Chicago Lying In Hospital, affiliated with the University of Chicago.

the localization of metallic foreign bodies. For that work simple (non-stereoscopic) triangulation as illustrated by Sweet and Strohl localization methods was at least as satisfactory as the stereoscopic triangulation employed by MacKenzie Davidson.[7] However, where the parts to be identified are projections and ridges on living bone rather than dense metallic objects, stereoscopic vision becomes an important aid to accuracy.

STEREOSCOPIC TRIANGULATION

Three distinct steps are involved in the measurement of pelvic diameters by stereoscopic triangulation:

(1) The patient must be positioned so that the shadows of obstetrical landmarks may be readily identified on the film. (Not to be confused with the situation in the position methods where relationship of subject and film not only influences visibility of landmarks but also enters directly into the validity of the computations.)

(2) Measurements of target-film distance and tube shift must be known with considerable accuracy. The relationship of mean tube position and film center must be known and the plane of tube shift must be parallel to the plane of the film.

(3) The films must register and computations must be made either by means of tables and formulae or with the aid of mechanical devices.

After studying the scanty literature on this particular phase of roentgen-ray pelvimetry, we have decided to employ certain features of the work of Manges,[27,28] Chamberlain and Newell,[6] and Johnson,[22–25] together with a modification of the semi-recumbent position of Fabre and Thoms.

Manges in 1911 applied MacKenzie Davidson's cross-thread method to the study of stereoscopic pelvic roentgenograms and felt that he could measure any pelvic diameter with great accuracy. Potter-Bucky grids had not been developed at that time and the problem of obtaining sharp images was very great, particularly late in pregnancy. The recumbent position was used and it was seldom possible to identify the sacral promontory.

Chamberlain and Newell in 1921 published a method that utilized a commercial tube stand and accomplished registering of the films and an accurate knowledge of the two positions of the target by means of a plumb bob hanging from the tube and centered by preliminary roentgenoscopic observation. Calculations were made either with a special scale rule or by means of formulae involving squares and square roots. The method has been little used by others, possibly because of the degree of care that must be exercised at the time the films are being made.

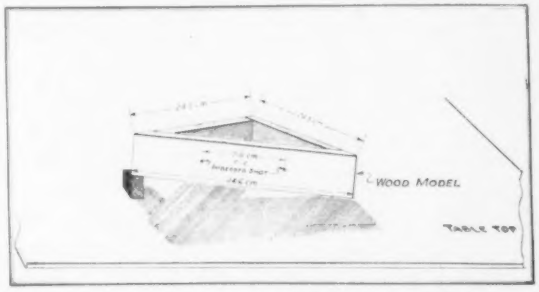


FIG. 2. Wooden model with lead shot imbedded in it exactly 12.6 cm. apart center to center.

Johnson, unacquainted with the work of MacKenzie Davidson and Manges, developed independently a cross-thread apparatus for the study of stereoscopic films, calling it a "stereoroentgenometer." This instrument consists of a horizontal viewbox carrying a vertical post equipped with a horizontal arm to which a pair of reels is attached. The eyes of these reels are accurately located so that their relationship to the plane of the view box is the same as the relationship of the two positions of the target to the roentgen film. Corresponding shadow points are identified on the films which are then superimposed on the viewbox. By means of calipers attached to wires from the reels a phantom geometric model is constructed, the wire from one reel passing in a straight line to the image made when the target was in that position, the second passing to the second image. The

crossing of the two locates the true position of the object in space. This position is recorded by means of an adjustable pointer and the process is repeated for as many

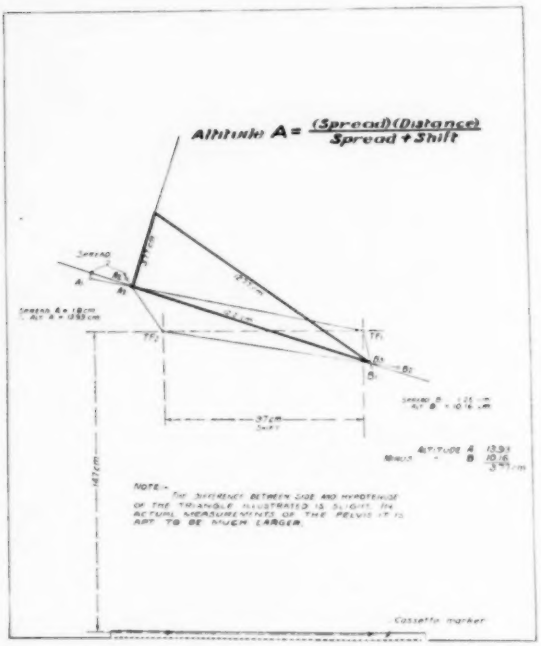


FIG. 3. Diagram of tracing from double-exposed film. For explanation see text.

other points in the pelvis as the examiner desires to study. By means of an ordinary metric rule spanning from one pointer to another, the true distance between any pair of points can be measured.

Films are registered by means of a marker attached to the Potter-Bucky grid tray but the careful adjustment of tube shift and target-film distance are matters that must be attended to by the examiner.

A SPECIAL OBSTETRICAL TABLE

We have at our disposal an obstetrical roentgen table (Fig. 1) equipped with a specially designed tube arm that pivots in the plane of the film. When tube arm and Potter-Bucky grid are locked to their tracks with their pointers at corresponding points on two centimeter scales, the arm standing at 90° with the table top, the target of a Metalix roentgen tube lies perpendicularly above the center of the film and slightly more than 89 cm. from its surface. When the arm is angulated 3° away from perpendicular, target-film distance becomes exactly 89 cm. and a perpendicular dropped from this position of the target strikes the central axis of the film exactly 4.85 cm. away from the center. A bolt is provided so that when the table is being used for pelvimetry, angulation is limited to 3° each way from center or a total of 6°.

By this means we are able to make stereoscopic roentgenograms with a target film distance of exactly 89 cm., a tube shift of exactly 9.7 cm., the plane of the tube shift exactly parallel to the plane of the film and the relationship between film center and target positions known. The accuracy of these relationships has been checked by precision machine shop methods and does not depend upon the efforts of the person making the roentgenograms.

FILM REGISTERING MARKER

A marker somewhat similar to the one described by Johnson is attached to the Potter grid tray. It consists of a strip of lead reinforced with brass and pierced by two small drill holes exactly 9.7 cm. apart center to center. These holes photograph as black dots on the film edge 9.7 cm. apart and 14.7 cm. from the central axis of a 10″ by 12″ roentgen film. In 14″ by 17″ films the distance is 17.3 cm. Actually, of course, the dots are slightly farther apart than the drill holes and slightly displaced from perpendiculars dropped through the center of the drill holes to the surface of the film but the lead is so close to the film that the error is negligible. We have demonstrated this fact to our own satisfaction by experiments.

THEORY OF MEASUREMENT BY TRIANGULATION

A simple wooden model (Fig. 2) has two lead shot imbedded in it, 12.6 cm. apart center to center. This model was positioned on the table top so that the shot were at different distances from the surface of the

film and then two exposures were made on one film, the tube being angled 6° between exposures. Figure 3 is a tracing of the film thus obtained, showing one image of each of the drill holes in the film marker and two images of each of the shot. By drawing a line through the black dots on the film edge, erecting perpendiculars through the dots and then measuring out 14.7 cm. along these perpendiculars we locate points on the film perpendicularly below the two positions of the target. These we designate "target foot points" and label them TF_1 and TF_2.

A_1 and A_2 are two images of one of the shot, A_1 being cast by radiation coming from above TF_1, A_2 from above TF_2. B_1 and B_2 are shadows of the second shot.

In Figure 4, T_1, A and A_1 are points lying in a straight line intersecting the plane of the film U. V. at the point A_1. If TF_1 represents the foot of a perpendicular dropped from target position T_1 to the plane U.V., then Y constitutes a straight line in that plane and a perpendicular dropped from A to the plane U.V. must intersect Y. By the same reasoning A_3, the foot point of the perpendicular dropped from A, lies on a line connecting TF_2 and A_2. It follows, therefore, that it must lie at the intersection of these lines.

By inspection one can always determine which shadow of A was cast from T_1, which from T_2 but when A_3 lies in or near the midline it may not be possible to locate A_3 by constructing the lines TF_1A_1 and TF_2A_2 and noting their point of intersection.

In such cases A_3 may be located by substituting in a formula, solving for X and measuring off this distance from A_1 along the line Y,

$$X = \frac{(\text{altitude } A)\ Y}{K}$$

where

X = Distance on film between A_1 and A_3 along Y

Y = distance on film between TF_1 and A_1

Altitude A = Perpendicular distance from point A_3 on the film to the location of the object A in space

K = Target film distance (in this case a constant 89 cm.)

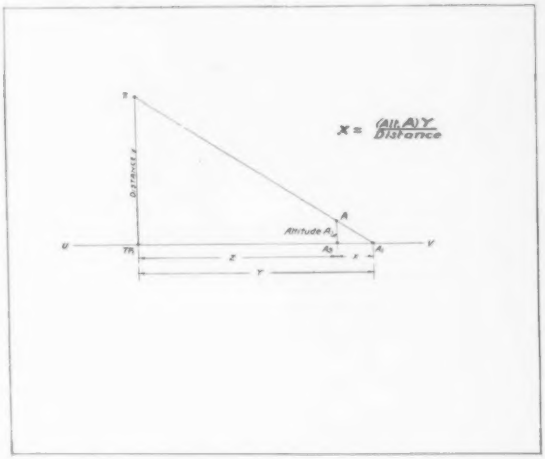


Fig. 4. Diagram illustrating the similar triangles that are formed when lines are drawn connecting location of roentgen target and film, position in space occupied by lead shot and shadow of shot on film, etc.

This formula is obtained easily from Figure 4 where we see that the triangles T_1, A_1, TF_1 and A, A_1, A_3 are similar. It follows, therefore, that $\frac{\text{DISTANCE}}{\text{ALTITUDE } A} = \frac{Y}{X}$ and by transposition $X = \frac{\text{Altitude } A\ (Y)}{\text{DISTANCE}}$.

A NOMOGRAM FOR ESTIMATING THE LOCATION OF A_3

The only computations involved in solving for X are multiplication and division which may be done on a slide rule. They may be done more conveniently, however, by means of a nomogram that has been prepared for us by Mr. Youtz of the Department of Mathematics (Fig. 5). A thread is stretched from any value of altitude A in the left column to any value of Y in the right column and at the intersection of the thread with the middle line the value of X is read directly in cm.

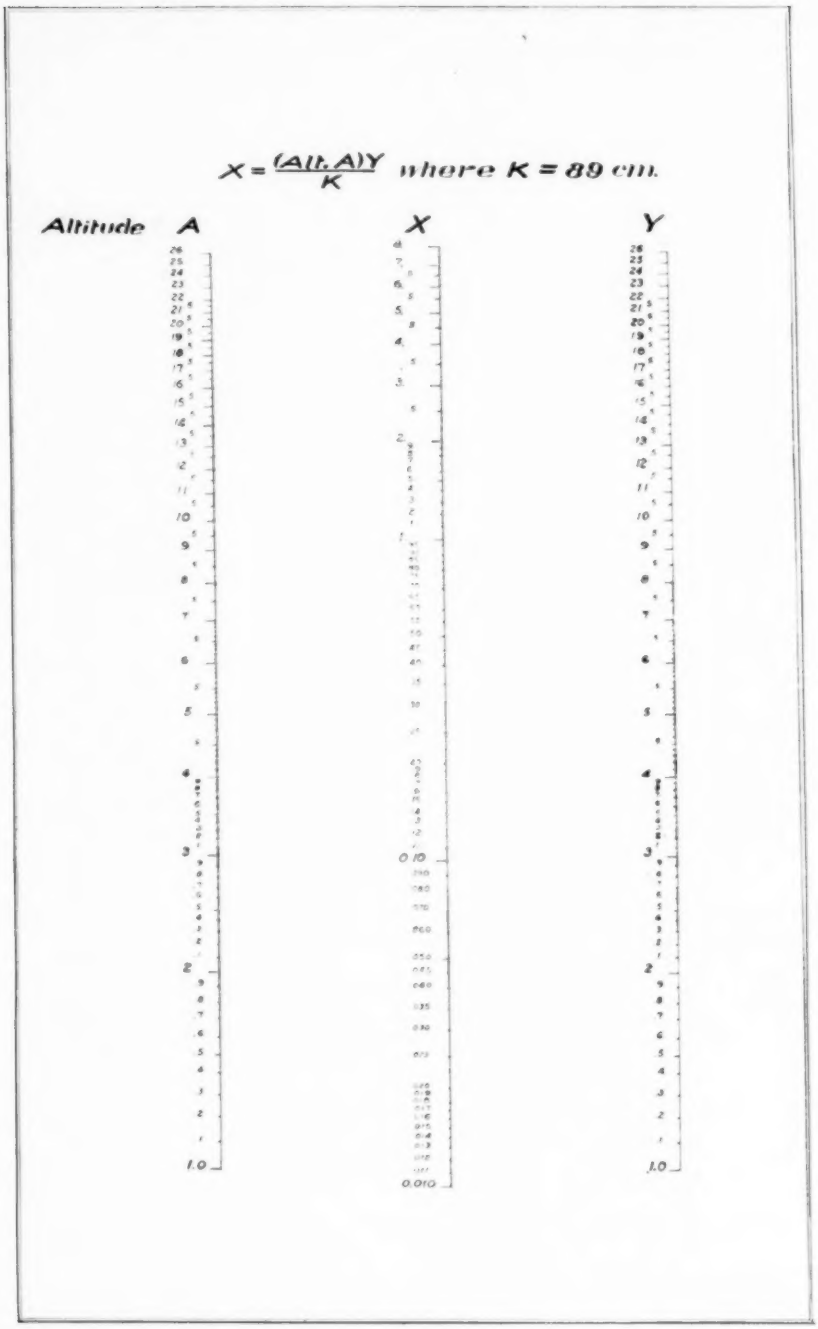


FIG. 5. Nomogram used in locating A_3, B_3, etc., in midline objects. Measure the distance on the film between any shadow point and its corresponding target foot point. Locate this value on the Y scale of the nomogram. Estimate the altitude of the object that casts the shadow and lay off this value of the Altitude A scale. A thread stretched between these points gives a value for X in centimeters. Measure off this distance from the shadow point along the line drawn to its target foot point. The end of the line thus constructed constitutes the point A_3 which is the foot point of a perpendicular dropped from the object to the plane of the film.

FORMULAE AND TABLES FOR ESTIMATING ALTITUDE A, ALTITUDE B, ETC.

The equation $\frac{\text{DISTANCE}}{\text{Altitude } A} = \frac{Y}{X}$ may be re-written Altitude $A = \frac{(\text{DISTANCE})\ X}{Y}$ but by construction $Y = X + Z$, therefore Altitude $A = \frac{(\text{DISTANCE})\ X}{X+Z}$.

This equation is sometimes capable of solution because DISTANCE is known (89 cm.) and except in the case of midline objects the other two values can be measured on the film. It could be made applicable to all cases, however, if it were possible to substitute SPREAD for the value X and SHIFT for the value Z because SHIFT (the distance through which the target of the roentgen tube is moved) is fixed at 9.7 cm. and SPREAD (the measured distance between the two shadows A_1, A_2) can be measured on the film regardless of the relationship of the objects to the midline. This substitution can be made. Figure 6 is a simplified drawing of part of Figure 3 showing two shadow points transferred from the double-exposed film, two target foot points and the lines connecting foot points and corresponding shadows. These lines describe another pair of similar triangles involving "SPREAD" and "SHIFT," X and Z. X and Z are similar, "SPREAD" and "SHIFT" are similar, so that

$$\frac{X}{X+Z} = \frac{\text{SPREAD}}{\text{SPREAD} + \text{SHIFT}}.$$

We may write, therefore, altitude $A = \frac{(\text{SPREAD})\ (\text{DISTANCE})}{\text{SPREAD} + \text{SHIFT}}$. It requires only a few hours' work with a modern calculating machine to reduce this equation to tables in which altitude A can be read off directly for all ordinary values of SPREAD. This we have done but it must be remembered that the tables are applicable only when DISTANCE is 89 cm. and SHIFT 9.7 cm.

Spread in Centimeters	Altitude A, B, etc. in Centimeters	Spread in Centimeters	Altitude A, B, etc. in Centimeters
0.10	.91	2.85	20.21
.15	1.36	2.90	20.48
.20	1.80	2.95	20.75
.25	2.24	3.00	21.02
.30	2.67	3.05	21.29
.35	3.10	3.10	21.55
.40	3.52	3.15	21.82
.45	3.95	3.20	22.08
.50	4.36	3.25	22.34
.55	4.78	3.30	22.59
.60	5.18	3.35	22.85
.65	5.59	3.40	23.10
.70	5.99	3.45	23.35
.75	6.39	3.50	23.60
.80	6.78	3.55	23.85
.85	7.17	3.60	24.09
.90	7.56	3.65	24.33
.95	7.94	3.70	24.57
1.00	8.32	3.75	24.81
1.05	8.69	3.80	25.05
1.10	9.06	3.85	25.29
1.15	9.43	3.90	25.52
1.20	9.80	3.95	25.75
1.25	10.16	4.00	25.99
1.30	10.52	4.05	26.21
1.35	10.87	4.10	26.44
1.40	11.23	4.15	26.67
1.45	11.57	4.20	26.89
1.50	11.92	4.25	27.11
1.55	12.26	4.30	27.34
1.60	12.60	4.35	27.56
1.65	12.94	4.40	27.77
1.70	13.27	4.45	27.99
1.75	13.60	4.50	28.20
1.80	13.93	4.55	28.42
1.85	14.26	4.60	28.63
1.90	14.58	4.65	28.84
1.95	14.90	4.70	29.05
2.00	15.21	4.75	29.26
2.05	15.53	4.80	29.46
2.10	15.84	4.85	29.67
2.15	16.15	4.90	29.87
2.20	16.45	4.95	30.07
2.25	16.76	5.00	30.27
2.30	17.06	5.05	30.47
2.35	17.36	5.10	30.67
2.40	17.65	5.15	30.87
2.45	17.95	5.20	31.06
2.50	18.24	5.25	31.25
2.55	18.53	5.30	31.45
2.60	18.81	5.35	31.64
2.65	19.10	5.40	31.83
2.70	19.38	5.45	32.02
2.75	19.66	5.50	32.20
2.80	19.94	5.55	32.39

Spread in Centimeters	Altitude *A*, *B*, etc. in Centimeters	Spread in Centimeters	Altitude *A*, *B*, etc. in Centimeters
5.60	32.58	6.15	34.53
5.65	32.76	6.20	34.70
5.70	32.94	6.25	34.87
5.75	33.12	6.30	35.04
5.80	33.30	6.35	35.21
5.85	33.48	6.40	35.38
5.90	33.66	6.45	35.54
5.95	33.84	6.50	35.71
6.00	34.01	6.55	35.87
6.05	34.19	6.60	36.04
6.10	34.36		

TESTING THE FORMULA

In Figure 3 SPREAD measures 1.8 cm., so from the tables the altitude of *A* is 13.93 cm. Altitude *B* works out at 10.16 cm. If we were to construct a plane parallel to the plane of the film and passing through the shot *B*, it would cut the perpendicular from *A* 10.16 cm. above the film or 3.77 cm. below the other shot. A line drawn in this new plane joining the perpendiculars from *A* and *B* is identical in length with the line A_3B_3 and the straight line distance between shot *A* and shot *B* is the hypotenuse of a right triangle, the other two sides of which are identical with the length of the line A_3B_3 and the difference between altitude *A* and altitude *B*.

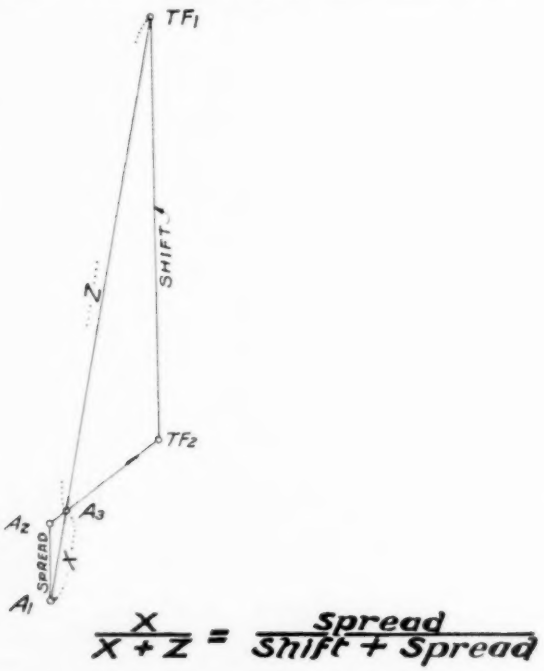


FIG. 6. Part of Figure 4 redrawn to show that its similar triangles are related to those of Figure 5.

This triangle has been constructed on the film tracing (It must be remembered that the tracing is used merely as convenient work paper and that the figure is not a perspective drawing.) and measurement of the hypotenuse AB_3 gives a value of 12.77 cm., which closely approximates the true distance between the lead shot (see description of the model and Figure 2).

If several pair of points are being worked out on a single tracing, it may be confusing to draw triangles. In such cases one may use a sheet of millimeter cross-section paper, laying off the measured distance AB_3 on one axis of the paper, the difference between altitude *A* and altitude *B* on the other axis and measuring the hypotenuse directly with a metric rule.

RE-STATEMENT OF GENERAL PRINCIPLES

To measure the straight line distance between shot *A* and *B*, using the information from the double-exposed film (Fig. 3) proceed as follows:

1. Measure SPREAD *A* and SPREAD *B*.
2. Using tables, compute altitude *A* and altitude *B*.
3. By construction or by means of the nomogram, locate A_3 and B_3.
4. By sketching on the tracing or by means of cross-section paper, construct the right triangle and measure its hypotenuse.

MEASUREMENTS OF OBJECTS BY MEANS OF STEREOSCOPIC FILMS

The double-exposed film provides a simple illustration of the principles of measurement by triangulation but its images are fogged and where the material under study is human tissue rather than dense lead shot the film is unreadable. To overcome this difficulty one has merely to substitute for the double-exposed film a pair of stereoscopic films; identify corresponding points on each and transfer these points to a sheet

Fig. 7. Tracing paper used to transfer shadow points from stereoscopic films. The central dots are target foot points. Circles near the edge of the sheet are register points for 14″×17″ films. The pair of circles lying nearer the center of the sheet are register points for 10″×12″ films.

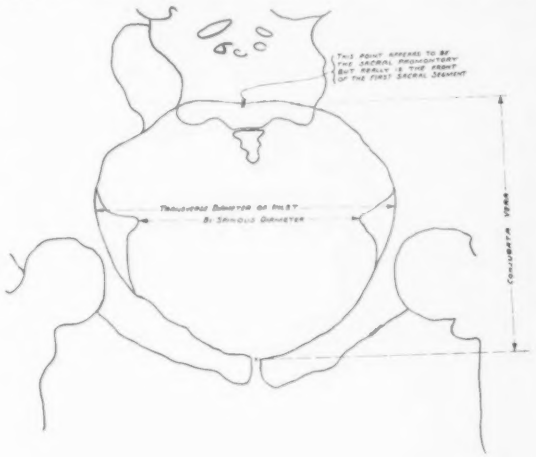
of paper. We use for this architect's tracing paper printed to show positions of TF_1 and TF_2 relative to the register points on either 10″ by 12″ or 14″ by 17″ film (Fig. 7). Manges and Chamberlain employed somewhat similar tracing sheets and Johnson accomplished the same purpose by superimposing the two films on the viewbox of his stereoroentgenometer.

The films are first studied in a stereoscope where the points in question are marked with a wax pencil. The tracing paper is then registered over the first film and pencil dots made at the site of the wax pencil marks. This is repeated for the second film, following which the tracing is treated as in Figure 4 where it was made from a single film double exposed. Employing this two-film method and using only a moderate degree of care, we have been able to measure the distance between the shot in our wood model with a surprising degree of accuracy. The problem is simple as long as the corresponding shadow points can be clearly identified in both films.

MEASUREMENTS OF THE DRIED PELVIS

When one undertakes to measure the obstetrical diameters of a dried pelvis, to say nothing of the pelvis of a living subject late in pregnancy or the skull diameters of a full-term fetus, it becomes vastly more difficult to identify shadow points. The position of the subject is an important factor. Figures 8 and 9 are tracings of films of a dried pelvis showing the actual caliper measurement of certain diameters together with the value of the diameters computed from stereoscopic films. The sitting position is obviously to be preferred to the recumbent when one wishes to identify the sacral promontory. In fact, in the living subject, particularly late in pregnancy, it is seldom possible to make out this point in recumbent-position films.

Note, however, that there is an error of approximately a centimeter in estimating


THIS POINT APPEARS TO BE THE SACRAL PROMONTORY BUT REALLY IS THE FRONT OF THE FIRST SACRAL SEGMENT
TRANSVERSE DIAMETER OF INLET
BI-SPINOUS DIAMETER
CONJUGATA VERA

TRACING FROM FILM OF DRIED PELVIS IN SITTING POSITION

10.6 cm. ACTUAL C.V.
11.75 cm. COMPUTED C.V. (ERROR IN LOCATING SACRAL PROMONTORY)
11.2 cm. ACTUAL BI-SPINOUS DIAMETER
11.4 cm. COMPUTED BI-SPINOUS DIAMETER
13.9 cm. ACTUAL GREATEST DIAMETER OF INLET
13.85 cm. COMPUTED GREATEST DIAMETER OF INLET

Fig. 8. Tracing from film of dried pelvis in sitting position. In this particular case the promontory does not show, the point marked being really the anterior surface of the first sacral segment. An error of about 1 cm. in estimating conjugata vera results.

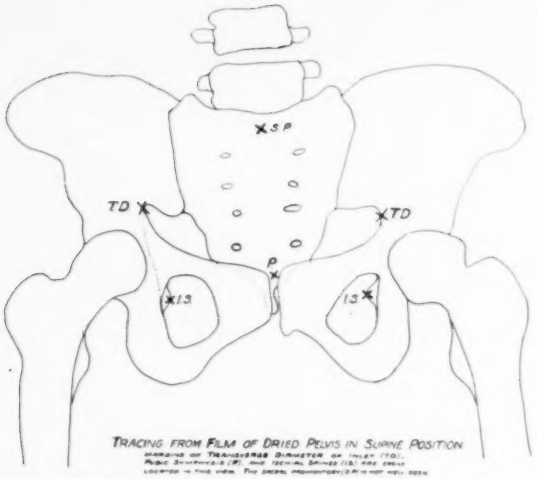


FIG. 9. Tracing from film of dried pelvis in recumbent position.

the conjugata vera, an error that has persisted in three independent examinations. The explanation appears to lie in the fact that the point selected by us and shown on the tracing as representing the sacral promontory is really the anterior surface of the concave front of the first sacral segment.

We consider the point important and believe that one must be skeptical of his ability to make out the sacral promontory in sitting-position films of living subjects.

MEASUREMENTS OF LIVING SUBJECTS

The accuracy of the stereoscopic method unlike that of the frame methods does not depend, *per se*, on the relative positions of subject and film but if we are to attempt accurate measurement between shadow points by any method, it is obvious that we must be able to see the points clearly.

By placing a living subject in the semi-recumbent position one obtains a film (Fig. 10) in which the pelvic inlet is visualized almost as well as in the case of the dried pelvis. We have examined a good many non-pregnant subjects in this position but have not yet had the opportunity to check the measurements at autopsy. However, our experiment with the dried pelvis (Fig. 8) leads us to suspect an error in the measurement of the conjugata vera.

While the semi-recumbent position is useful and practical in the non-pregnant subject or early in pregnancy it cannot always be employed when subjects are near term.

The principal difficulty lies in the fact that the position interposes a large amount of uterine and fetal tissue between roentgen tube and the cephalic half of the film with resulting blurring and underexposure of the sacral promontory. Furthermore, a knowledge of the diameters of the fetal head may be desired and fetal parts are usually seen best with the subject recumbent (Fig. 11).

The lateral position (Fig. 12) allows accurate identification of the sacral promontory in all cases but, unfortunately, details of the pubic symphysis in films of the living pregnant subject are not nearly as clear as one might judge from this tracing of the film of a dried pelvis. We have experimented a little using an aluminum clamp carrying a lead shot that can be introduced into the vagina and held in position against the posterior surface of the pubic symphysis. This provides an admirable landmark in the films and its design could probably be modified to allow

FIG. 10. Roentgenogram of pelvis made with the living subject in the sitting or semi-recumbent position. Sacral promontory, pubic symphysis, ischial spines and lateral margins of the inlet appear to be well shown. Experiments with the dried pelvis indicate that the prominent bulge at the posterior margin of the pelvis may not always be the sacral promontory.

painless, fairly accurate insertion by a physician not especially trained in obstetrics. On the other hand, the instrument must be applied after the subject has been positioned on the roentgen table so that aside from the risk of injury to the patient there is the further disadvantage that the attendance of a physician is required at the time the films are being made.

MEASUREMENTS ON ANATOMICAL AND AUTOPSY MATERIAL

Except for the dried specimens we have not as yet been able to check the accuracy of our measurements of human tissue. A special table has been constructed much simpler than our clinical instrument but embodying the essential features of fixed target film distance and tube shift and built-in film registering marker, and some measurements have been attempted. However, all of the cadavers so far studied are found to be injected with radiopaque material that fills abdominal and pelvic vessels and obscures the field. Autopsy material offers more promising possibilities but this work has barely begun and the two cases thus far studied proved unsatisfactory—in one instance because of metastasis to the pelvic bones that destroyed pelvic landmarks, and in the other case because of an enormous liver that obscured the upper half of the film.

Tracing from Film of Living Pregnant Subject in Supine Position

Fig. 11. Tracing from roentgenogram of pregnant subject at full term in recumbent position. This is perhaps the best general purpose view of the pregnant abdomen and pelvis but it seldom allows accurate localization of the sacral promontory.

Tracing from Film of Dried Pelvis in Lateral Position
10.6 cm. Actual C.V.
10.6 cm Computed C.V.

Fig. 12. Tracing from lateral roentgenogram of dried pelvis. This view is excellent for the sacral promontory but in the living subject the pubic symphysis is seldom well seen.

A number of clinical and anatomical problems suggest themselves but in all of them the principal difficulty will lie in the clear visualization of the points in question on the roentgen films. Whenever points can be clearly identified the distance between them can be measured accurately regardless of the position of the patient or the relationship of the structure to the film.

CONCLUSIONS

A method of pelvimetry by stereoroentgenography is described in considerable detail with illustrations and explanations of each of the three stages that are involved.

(1) The matter of optimum position of subject remains debatable, the recumbent, semi-recumbent and lateral positions each having advantages and disadvantages from the standpoint of adequate visualization of obstetrical landmarks.

(2) No special professional ability is required of the person making the films, target-film distance and tube shift being fixed by the mechanical design of the roentgen tube stand and table. The apparatus is not designed exclusively for pelvimetry, however, but may be used for practically any type of roentgen examination.

(3) Johnson's stereoroentgenometer is recognized as the simplest and most satisfactory device for making the computations but to illustrate the principles involved and make the method available to laboratories not equipped with Johnson's instrument, tables and a nomogram are published. These are believed to be simpler and capable of more rapid application than previously published formulae.

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DISCUSSION

Dr. Henry J. Walton, Baltimore, Md. I feel that Dr. Hodges and Dr. Ledoux are to be congratulated upon the very excellent work they are doing. It is to be hoped that as they proceed with their experiments, their method may be simplified so that it can be used by roentgenologists in general. They are working in a diagnostic field which I believe is destined to become as important as any in which the roentgen rays are now being used.

When one considers that over 20,000 women die each year during childbirth in this country alone, it would naturally be expected that any adjunct which would tend to lessen this mortality would promptly receive general acclaim by the medical profession. But so many superstitions have been associated with childbirth from time immemorial that it is difficult to break away from established customs.

By a routine roentgen examination, the roentgenologist can now obtain more information regarding the size, form and position of the fetus in utero and the relationship that the head of the child bears to the pelvic canal than the obstetrician can possibly tell by his most careful and painstaking examinations extending possibly over months of observation.

As 60 per cent of the deaths during parturition are due to puerperal infection or its complications, by eliminating the necessity of a vaginal examination there would necessarily follow a marked decrease in this tremendous mortality. I believe the time is not far off when the roentgen examination will be a routine procedure in practically every case of pregnancy.

Dr. Hodges has worked out a very exacting technique for measuring the head and pelvis, and in doing so has doubtless claimed the attention of many of his associates, especially those interested in obstetrics. His method is probably too complicated for the average roentgenologist, but if it proves practical in his hands, it means a step forward in the establishment of the roentgen examination as a routine diagnostic procedure in pregnancy.

Dr. Willis F. Manges, Philadelphia. It would be a splendid accomplishment if it were possible for all of us to measure accurately the

female pelvis. It would be a good thing if we could do it long before, or at least well before, the stage of childbirth. Accurate measurements in the later stages of pregnancy are relatively unimportant, largely because of variations in size of fetal heads. One lady has a seven-pound baby, another has a nine-pound baby, and some are even proud of larger ones. So that unless we can establish, by means of very accurate measurements average pelvic diameters in various directions, that tell the obstetrician that his patient is not apt to have a normal labor, regardless of the size or position of the fetus, we won't accomplish much.

I measured the pelvis with extreme accuracy as far back as 1910 and 1911, proved it from dried pelves and anatomical specimens and adapted it to the living. My method was extremely simple. At that time some of you may remember the old table that had the two uprights and a bar across on which the tube was supported and on the under surface of that tube holder we had a localizing apparatus that we could attach. By means of that localizing apparatus, we used to localize foreign bodies in any other portion of the body. I used that for localizing various points on the pelvic brim. I could localize those spots that I made on the stereoscopic films in pencil, having them checked first on one film and then the other, and do it with extreme accuracy. If you didn't have a Snook table and you weren't of a mind to use a localizing apparatus, it wasn't any good to you. The method never was practical on any but this one table, which has been discarded long ago.

Now Dr. Hodges comes with a special table by means of which he can probably make an accurate measurement. I don't believe that this is just the right step to take for as important a thing as this. We have got to devise some means of measuring the female pelvis with apparatus that all of us have. We can't all buy obstetrical tables. We can't have a separate room for this particular work.

What I am coming to is this, that I believe methods like Dr. Walton uses, having a chart that allows for variation of the images at different distances from the film, are practical. Everybody can use them. They are easily used and they are practically accurate, if not mathematically so. After all, the best information that we give the obstetrician is at the time or near the approach of childbirth to determine the relative size of the pelvis and the head of the fetus, the position of it and that sort of thing. A difference of half a centimeter in any diameter of the pelvis isn't the thing that comes right down to the final issue and makes the important issue at the time of labor.

DR. HODGES (closing). Dr. Manges' discussion is based on my verbal presentation of a hurried abstract of our paper, a form of presentation rendered necessary because papers presented earlier in the morning took up practically all of the time originally allotted to us. In our complete publication Dr. Manges will find that we are acquainted with his work published twenty years ago and have borrowed from it. We are confident, however, that if he were to become interested again in pelvimetry he would not be content today with facilities that seemed so excellent nearly a quarter of a century ago. Debate on the question as to whether the position methods are after all "accurate enough" seems futile until we know how accurate they are.

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THE DEMONSTRATION OF VESICAL CALCULI BY ROENTGENOGRAPHY*

By HERBERT A. JUDSON, M.D.
LOS ANGELES, CALIFORNIA

IT IS well known that a certain number of stones in the kidney and gall-bladder fail to show upon roentgenologic examination and the same belief is generally held with respect to stones in the urinary bladder. A review of the literature does not reveal any figures as to what percentage of vesical calculi are not shown by roentgenography, though there are articles, chiefly in the European journals, reporting non-opaque stones.

Having access to 88 stones removed by operation from the urinary bladder of patients in a district in South China, it was thought it might be interesting to subject these stones to roentgenographic tests, to determine: (1) How many of them might have been expected to show by ordinary roentgen examination, (2) what factors might be an aid in rendering more easily visible the less opaque stones.

To this end a phantom was prepared, as follows: An aluminum kettle with a bottom about 2 mm. thick, was filled with tap water to a depth of 18 cm. A layer of gauze was stretched across the kettle at a depth of 10 cm. from the bottom, the stones being placed upon the gauze. Exposure was made as for an ordinary film of the vesical area of a medium-sized patient, with cone, screen and Potter-Bucky diaphragm.

Water was used as a medium because of its convenience and because it so nearly approximates the density of body tissue. If the density of water is 1, the density of fatty tissue may be given as 0.97, of blood 1.03, of muscle 1.05.[1] The atomic number of water is 7.6. The atomic number of the elements that make up body tissue is about the same, being between 7 and 8. Twenty centimeters is usually given as the average thickness of the adult pelvis; 18 cm. was considered a better average for these stones, both to make partial allowance for the alluminum in the bottom of the kettle, and also because the Cantonese are a smaller people. In addition, many of these stones were removed from children.

As a control, 66 gallstones were exposed, which had been removed by operation from a large adult. Six films of the gall-bladder region of this patient, previous to operation, had shown only one stone on five films, one other film showing three stones. When placed in the phantom and exposed, the film faintly showed these three stones but not as plainly as they were shown on the film of the patient. If the phantom was in error it would appear to be more on the side of not showing the stones as plainly as they were shown in the patient.

Of course, there are obvious fallacies in this type of experiment. In the first place, these are all Chinese stones and their composition might be quite different from that of the stones found in the United States. Wells[5] states, "Apparently there are marked differences in the prevailing composition of calculi in different countries; in China, for example, Pfister found 11 of 12 stones composed of uric acid." For South China there are reliable tables giving the chemical analysis of large numbers of bladder stones, and here the uric acid and urate stones unquestionably predominate.[3] Watson and Cunningham,[4] quoting from Sir Henry Thompson, give a table of analysis of 1,007 stones, whose composition does not differ greatly from that of the South China stones, but it is doubtful if their table applies directly to stones as found in this country. Recent observations would place calcium oxalate calculi as the more common urinary concretion here. Such stones are considerably more opaque to the roent-

* From the Department of Roentgenology, Massachusetts General Hospital, Boston, Mass.

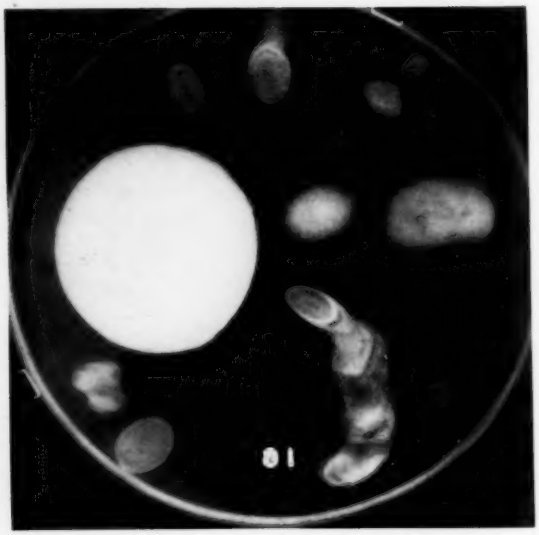

Fig. 1. This and the succeeding three figures are roentgenograms of 88 vesical calculi exposed in a water phantom with density approximating that of an adult pelvis. Each stone is plainly visible on the original films. There were 16 stones in this exposure.

gen rays than the uric acid stones and would make the average United States stone more easily visible than the average South China stone.

	South China Stones per cent	Watson and Cunningham Table per cent
Uric acid, and uric acid with phosphates	65	71
Phosphates	24	16
Oxalates, and oxalates with phosphates, and oxalates with urates	9	8
Miscellaneous (cystin, xanthin, etc.)	2	5

In the second place, 25 per cent of these stones being from children under ten years of age, and 18 per cent from patients between ten and twenty years of age, would tend to make them more easily visible in life than in the phantom. In this country, the majority of vesical calculi occur in much older individuals, 74 per cent of those removed at the Massachusetts General Hospital during the past seven years being from patients over fifty years of age.

Again, it does not fit the stone to the individual. There might be a small, soft stone in a very large individual. And there are other factors which make it impossible for a phantom ever to simulate exactly a living patient, as, for example, the fact that here we are making exposures under ideal conditions, a medium of uniform, homogeneous density, no motion whatsoever, etc. But recognizing these fallacies and realizing that no definite conclusions can be drawn, still the results obtained should be at least interesting and suggestive.

On the films exposed under these conditions, every one of the 88 stones is visible, as will be seen in the accompanying illustrations (Figs. 1 to 4).

Next, all the cases of vesical calculi found in the records of the Massachusetts General Hospital for the past seven years were reviewed, and the roentgenological findings checked in each case. The symptoms of stone in the bladder are as a rule so demanding of relief it is unlikely that any case would escape attention clinically, and so not be included in the records. These are the figures:

Total number of cases	48
Cases without roentgen examination	9
Total number of cases roentgenographed	39

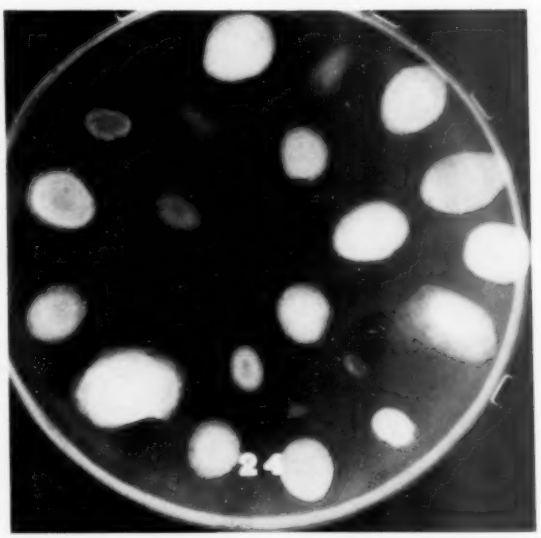

Fig. 2. There were 24 stones in this exposure.

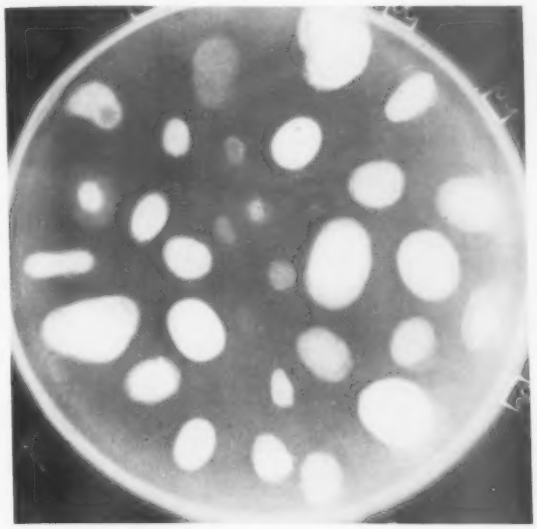

Fig. 3. There were 30 stones in this exposure.

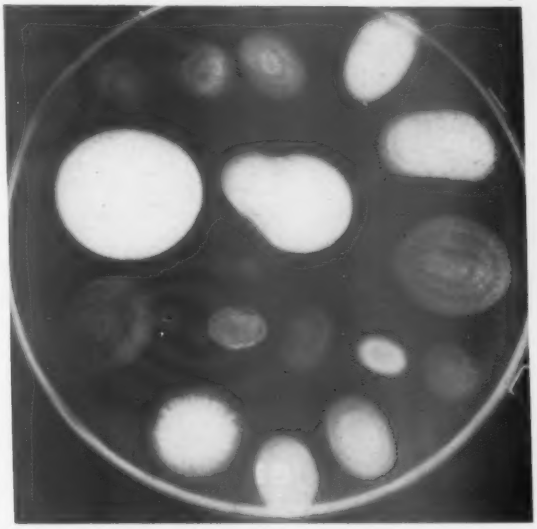

Fig. 4. There were 18 stones in this exposure.

Cases roentgenographed, with report positive for stone	37
Cases roentgenographed, with report negative for stone	2

The two cases with report negative for stone were then looked up. It was found that in each case a definite shadow was present, but had been attributed to other cause than stone. The area of increased density in the first case was thought to represent foreign material in the bowel. The second was a case of an unusually large, porous type of stone in a man aged sixty-four, where the shadow, although present, was not characteristic for stone. Figure 5 shows the unusual size and shape of the area and illustrates the difficulty there might be in recognizing such a shadow as a stone.

Probably the chief source of difficulty in roentgenologic diagnosis of vesical calculus is not so much in the demonstration of a shadow as in its correct interpretation. Thus fecaliths, foreign material in the bowel, calcified glands, calcification in uterine fibroids or other tumors or in the prostate gland, and phleboliths, may all be mistaken for calculus, or the shadow of an actual calculus may be interpreted as any one of these. This is especially likely to happen if the shadow is unusual in appearance or location, as for example, when present in a diverticulum.

In concluding this part of the experiment, it can be stated that (1) of 88 vesical calculi roentgenographed in a phantom approximating the density of an adult pelvis, every stone is visible; (2) of 39 cases of vesical calculi in the Massachusetts General Hospital during the years 1924 to 1930, inclusive, which also had roentgenographic

Fig. 5. A vesical calculus of unusual size and shape, offering difficulty in differential diagnosis.

examination, a stone shadow was demonstrated in each case.

The second part of the work done, as to what factors might be an aid in rendering more easily visible the less opaque stones, consisted in roentgenographing under different conditions, five of the stones, and comparing the clearness of the shadows on the different films. The stones were placed on the bottom of a thin aluminum kettle and exposed as follows:

1. Submerged in 4 cm. of tap water.
2. Submerged in 4 cm. of urine, sp. g. 1018.
3. Submerged in 4 cm. of urine with pus.
4. Submerged in 4 cm. of urine with blood.
5. Submerged in 4 cm. of water, with movement during exposure.
6. Submerged in 4 cm. tap water and covered with a sacral bone.
7. Stones placed in an air-containing rubber balloon, which was submerged in 4 cm. tap water.

The results can easily be foretold. Pus, blood and urine, being of practically the same density, the stones showed with equal clearness in all these media. Movement so blurs the outline that a faintly visible stone is almost blotted out. A heavy bone will obscure a very light stone, but does not hide the denser ones. A surrounding layer of air renders the stones more distinct.

Probably then, the best technique to show a vesical calculus by ordinary roentgenographic examination would be to have the bowels and bladder empty, tube slightly tilted to correspond to the pelvic inclination and so project the bladder region out from under the pelvis, and absolutely no motion during exposure. Having the patient lie face down might bring the bladder nearer the film in some cases. As regards the use of different media in demonstrating vesical calculi, Lower[2] states, "The value of the roentgenogram has been greatly extended by the use of media of varying densities. It formerly was considered impossible to demonstrate a pure uric acid stone by means of the roentgenogram; but today, as has been demonstrated by Nichols, by using media of varying density, practically any type of stone can be shown." Thus air inflation or injection of an opaque medium might help at times, but should rarely be necessary.

I believe it is justifiable to draw the general conclusion that, with proper technique, a very large majority of vesical calculi can be demonstrated by the ordinary roentgen examination.

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ACUTE PULMONARY EDEMA*

CASE REPORT

By FRED O. COE, M.D., *and* LAURENCE S. OTELL, M.D.
WASHINGTON, D. C.

THE case which we are about to report is of interest to us for two reasons, particularly. In the first place, roentgenological records of pulmonary edema, during and following the attack, are extremely rare. Figure 1 shows the appearance of the lungs during the attack. Figure 2 shows the lung fields to be entirely clear at the end of forty-eight hours.

In the second place, a study of Figure 1 gives us a different concept of the pathology of acute pulmonary edema than is usually described in textbooks. Apparently certain groups of alveoli become filled with fluid as indicated by the splotchy appearance on the film. The remaining alveoli, particularly those situated at the periphery, are air-containing.

FIG. 1.

FIG. 2.

CASE REPORT

J. P., male, colored, aged thirty-six, was admitted to Georgetown University Hospital on January 6, 1930, complaining of extreme dyspnea and expectoration of large amounts of frothy sputum.

Family History. Mother living and well. Father dead—cause not known. One sister living and well. Four children in good health.

Past Clinical History. Measles, mumps, and whooping cough. Influenza in 1918. Gonorrhea at age of twenty-one. Had hard sore on penis at same time. Treated by oral medication. Has been subject to frequent colds. Occasional attacks of shortness of breath, especially in the past year. Has also noticed a forceful heart beat, and pain in the precordium for past year. Nocturia three to four times.

Present Illness. Onset suddenly on January 6,

* From the Radiological Clinic of Drs. Groover, Christie, and Merritt and Georgetown University Hospital, Washington, D. C.

about 6 P.M., after a hard day's work shoveling coal. Began with shortness of breath and coughing up of large amounts of frothy blood-tinged sputum, which literally poured from his mouth and nose. This was followed by extreme weakness and precordial pain.

Physical Examination. On admission to the hospital temperature was 98.6° F., pulse 120, and respiration 40. The lungs showed evidence of being filled with fluid. Hard crepitant râles were heard throughout both sides. Only a cursory examination was made at this time, due to the patient's acute illness. It was noted, however, that there was a marked enlargement of the heart, and a diastolic murmur was heard in the second interspace on the left.

Clinical Diagnosis. Acute pulmonary edema, syphilitic aortitis with regurgitation. The patient was given supportive treatment and medication consisting of digifoline ampules, one every four hours, codein sulphate, gr. $\frac{1}{4}$, and cinchonidine salicylate, gr. 3, in ampules, one every three hours. On the next day, fifteen hours after admission, temperature was 102° F., pulse 120, and respiration 32. The patient was considerably improved, dyspnea was relieved and pain in the precordium had disappeared. Râles persisted in both lungs, particularly in the upper lobes. The heart appeared to be enlarged both to the right and left. There was an increase in retromanubrial dullness, more than would normally be expected at this age. The heart beat was forceful. A systolic murmur was heard at the apex, and a diastolic murmur at the base, heard best in the second left interspace. The peripheral pulsations were noticeably forceful. Pulse, Corrigan in type. Capillary pulsations could be elicited in the nail beds. Blood pressure 170/40. The physical examination, otherwise, at this time was essentially negative. Electrocardiogram showed inverted T2 and T3. Wassermann 2 plus, Kahn 4 plus.

Roentgenographic examination showed a marked diffuse enlargement of the heart, particularly in the region of the left ventricle. There was a definite dilatation of the aorta. Radiating out from the hila on either side, are areas of increased density reaching in places almost to the periphery, most marked, however, at the lung roots. In places there is a tendency towards coalescence. These shadows evidently represent localized accumulations of fluid in neighboring groups of alveoli. The appearance, however, is not unlike that of the usual changes seen in pulmonary congestion (Fig. 1).

On January 8, physical examination showed no evidence of any pulmonary involvement. Unfortunately, a roentgenogram was not taken at this time. On the next day, however, roentgenographic examination showed the lungs to be entirely clear with no evidence of any of the shadows previously seen (Fig. 2).

The course in the hospital was uneventful and the patient was discharged considerably improved on the eleventh day after admission.

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INTRAVENOUS UROGRAPHY AFTER MAYDL'S OPERATION FOR EXTROPHY OF THE URINARY BLADDER*

By R. SIMON, M.D.
Professeur Agrégé, University of Strasbourg
STRASBOURG, FRANCE

and

A. BRUNSCHWIG, M.D.
Fellow, National Research Council
WASHINGTON, D. C.

SINCE the introduction of uroselectan by von Lichtenberg and Swick, the field for roentgenological examination of the genitourinary tract has been considerably extended.

FIG. 1. Roentgenogram taken five minutes after intravenous injection of abrodil (slightly retouched). The pelves and ureters are seen. There has been excretion of the opaque solution into the colon.

FIG. 2. Roentgenogram taken forty-five minutes after intravenous injection of abrodil (slightly retouched). R, right uretero-colonic junction. O, accumulation of opaque solution in the colon about the transplanted trigone. C, C′, C″, opaque solution in the colon (reflux) present as far back as the hepatic flexure.

We performed intravenous urography in the case of a thirteen year old boy operated upon for extrophy of the urinary bladder according to the procedure of Maydl (1894). This operation consists in the implantation of the trigone into the sigmoid colon with resection of the remaining portion of the bladder. It is more easily performed than implantation of the isolated ureters and has the advantage of preservation of the sphincter muscles of the ureteral orifices, which regulate the excretion of urine and tend to prevent reflux.

During the days immediately following operation there were numerous liquid

* From Surgical Clinic A, Strasbourg, France. Director: Professor Rene Leriche.

stools, but these gradually decreased in number until at present, ten weeks after operation, there are only four a day. The patient is in very good condition and at no time has there been evidence of ascending infection.

Two months following operation, with the aid of Dr. Sichel intravenous urography was performed using abrodil. This substance was first used in Germany by Bronner and Schüller.[1] It appears to be definitely less toxic than uroselectan and may be used in smaller doses. Chemically it is sodium mono-iodo-methane-sulphonate. It is an odorless, crystalline, white, powder of high water solubility. Boiling for fifteen minutes does not decompose the substance.

Prior to the introduction of intravenous urography it was not possible to visualize roentgenologically the uretero-colonic junction following such operations as described above. However this can now be done, and the integrity of the transplanted ureters or trigone easily controlled should there be a question of this during any postoperative complication.

The dilatation of the ureters in the case reported cannot be explained.

The reflux of the opaque solution to the hepatic flexure indicates that not only the rectal and sigmoid portions but the entire colon serves as a reservoir for the urine.

[1] Bronner, H., and Schüller, J. Die Ausscheidungspyelographie mit Abrodil. *Deutsche med. Wchnschr.*, 1930, *56*, 1393–1394.

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WAVE FORM ANALYSIS BY MEANS OF THE ROENTGEN-RAY STROBOGRAPH*

By C. B. BRAESTRUP, B.S., P.E.
Physicist, Department of Hospitals, City of New York and Mount Sinai Hospital
NEW YORK CITY

IT HAS long been recognized that the voltage wave form of the roentgen apparatus has an important bearing upon the radiation output of the roentgen tube. Differences of more than 100 per cent may be found in the radiation intensities obtained with generators of different wave form but operating at the same milliamperage and at equal crest voltage. In the consideration of the ray quality the wave form factor is of even greater significance.

The shape of the voltage wave may be studied most accurately with the aid of the oscillograph which records graphically how the potential across the roentgen tube varies with respect to time during the cycle of the alternating current. Unfortunately, the high voltage used in roentgenology and particularly in roentgen therapy complicates oscillographic investigations of the tube potential. Large, costly multipliers are needed, and these must have extremely high resistance in order that their current consumption does not affect the operating characteristics of the generator. Many of the published oscillograms therefore do not represent the voltage wave form for the actual conditions used by the roentgenologist.

In order to avoid the above complications we developed a simple, portable apparatus by means of which the analysis, including the set-up, can be made within half an hour and at any desired tube voltage. The device is shown in Figure 1. It incorporates some of the principles of the spinning top used in roentgenography for checking timers, the synchronized shutter as described by Chamberlain and Newell as well as some of the features of the stroboscope used in electrical engineering.

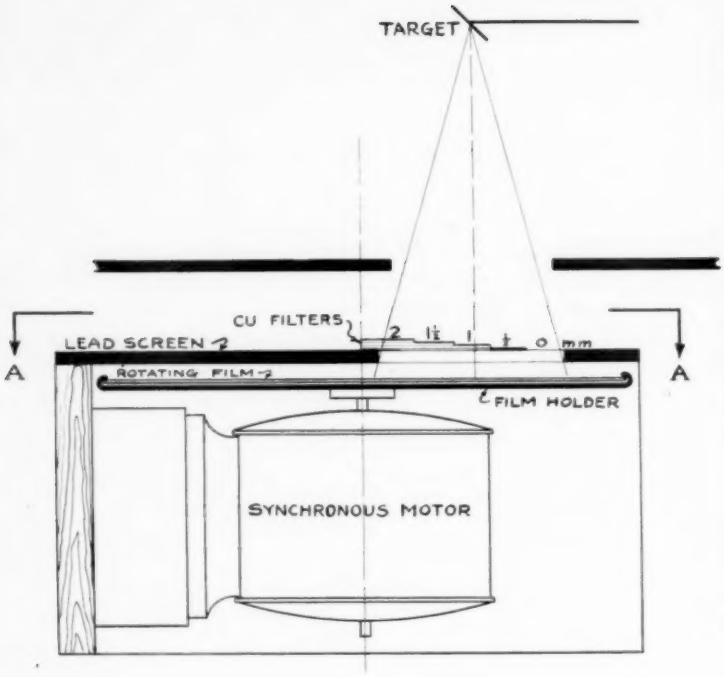
The apparatus consists essentially of a film rotating synchronously with the alternating current supply of the roentgen machine. By means of a lead screen provided with a wedge-shaped slit a small sector of the film may be exposed to a beam of roentgen rays. As the film revolves synchronously any position corresponds to a particular point of the alternating current cycle and in the case of mechanical rectification also to a definite position of the rectifying switch.

By means of suitable filters, each covering a part of the slit, beams of varying filtration reach the film. Due to the differential absorption of the short and long wave length radiation, the exposed film shows the variation in the ray quality during the cycle and thus analyzes, indirectly, the voltage wave.

In Figure 2 there is shown the analysis of a generator of the mechanical rectifying type where the tube voltage is pulsating and uni-directional. The radiation is in this case given off in pulses, each corresponding to one-half of a cycle or to an impulse. As the strobograph motor rotates 1,800 r.p.m. or 30 per second, the film indicates what takes place during two cycles or four impulses. The outer ring shows unfiltered radiation. The angle determined by the dark arcs indicates the part of the wave which is rectified. As the filtration is increased the angle of each arc becomes smaller. This shows that with increased filter thickness only the radiation produced at the crest of the voltage wave is used therapeutically.

Figure 3 is a strobogram made with a tube operating at so-called constant potential. The uniform density of each ring clearly shows that the variation in voltage or the ripple is small. Even the ring repre-

* Extract of paper read before the New York Roentgen Ray Society May 18, 1931. From the Radiotherapy Department of the Mount Sinai Hospital and the Division of Cancer, Department of Hospitals, New York City.



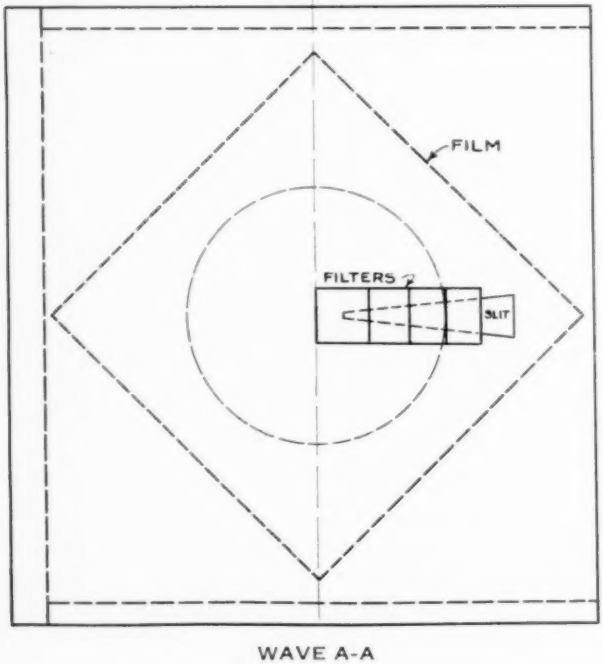


FIG. 1. Cross-section and top view of roentgen-ray strobograph. The device is shown with the film in a horizontal position. It can also be used with a film placed vertically. The angle of the slit is 4 degrees. The film is 8″×8″.

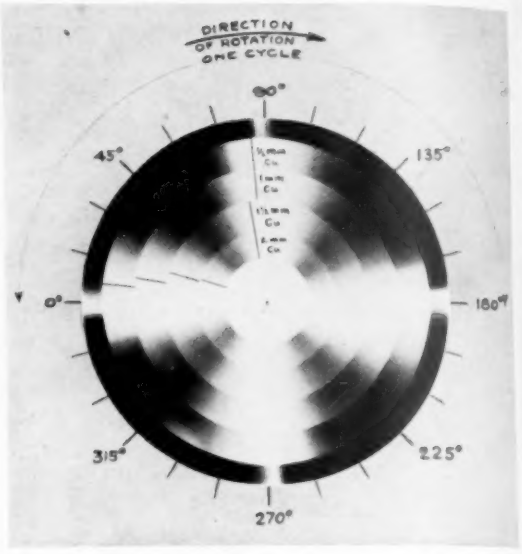


FIG. 2. Strobogram of mechanically rectified apparatus. Technique: 200 kv. max., 4 ma., target film distance 50 cm., time 15 minutes.

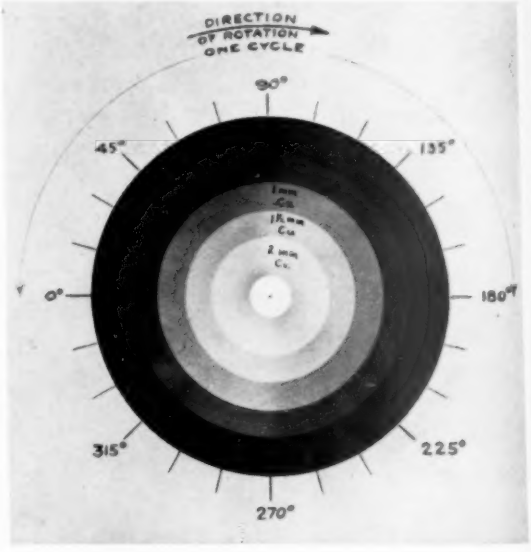


FIG. 3. Strobogram of "constant potential" valve tube apparatus. Technique: 180 kv., 4 ma., target film distance 50 cm., time 8 minutes.

senting 2 mm. of copper is quite uniform and with this filtration the slightest variation in potential would cause a visible change in the density. Closer examination of the original film discloses that there is a minute difference in density between alternate impulses. This may be explained by a slight unbalance of the rectifying system caused by a difference in voltage drop of the two valve tubes.

The last exposure, Figure 4, is taken with another type of high-voltage valve tube apparatus. It will be observed that the radiation here is practically given off only during every other impulse. It is also evident that a part of the radiation is produced at lower potentials resulting in diminishing arcs as the filtration is increased. In order, therefore, to obtain the same ray quality as with the constant potential generator a higher crest voltage must be used for equal filtration. However, compared with the mechanically rectified apparatus as analyzed in Figure 2 a lower maximum voltage of either type of valve tube equipment will produce equal ray quality at the same filtration.

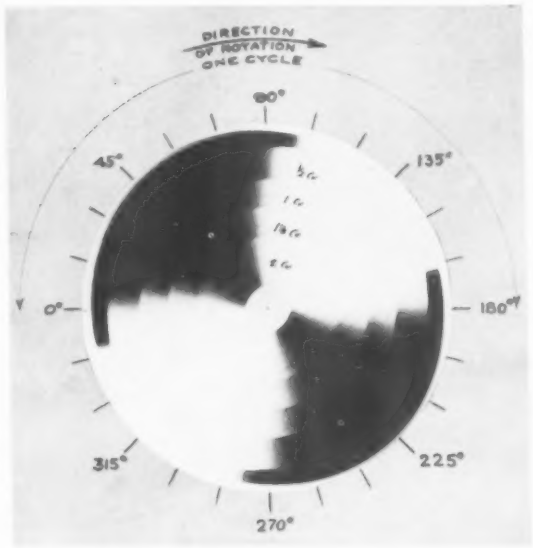


Fig. 4. Strobogram of sinusoidal potential valve tube apparatus. Technique: 180 kv. max., 4 ma., target film distance 50 cm., time 12 minutes.

SUMMARY

The described apparatus offers a simple means of analyzing the quantitative and qualitative variation of roentgen radiation during the cycle of the alternating current supply. Indirectly it also gives the voltage form of the generating equipment. The device is a useful tool in the detection and correction of improper rectification whether thermionic or mechanical.

Further experimentation is now being carried out with the aim of correlating the strobographic and oscillographic investigations of the voltage wave form with the ionometric measurements of the radiation.

The writer wishes to express his appreciation to Mr. Irving Blatz for his assistance in carrying out the experimental work.

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EDITORIALS

In Memoriam

PRESTON M. HICKEY
1865-1930

AS A mark of respect and deep regard for the memory of Dr. Preston M. Hickey, the American Roentgen Ray Society presented to the University of Michigan a silver bas-relief in commemoration of his services to science and also his great contribution toward the advancement of roentgenology. The presentation exercises were held in the Lydia Mendelssohn Theater at Ann Arbor on the afternoon of December 10, 1931, in the presence of the President of the University, who presided, the representatives of the Faculty of the Medical School and a host of friends and acquaintances, together with representatives of the American Roentgen Ray Society. The following addresses were delivered:

PRESTON M. HICKEY, PIONEER IN ROENTGENOLOGY

By A. W. CRANE, M.D.,
Onetime President, American Roentgen Ray Society

PRESTON M. HICKEY spent the best years of his professional life on a medical frontier. He knew its privations, toil and dangers, as well as its uncertain joys and finally its reluctant rewards.

Some great discoveries in medicine have elevated us to new viewpoints; others have opened up large new territories. Virchow broke into the land of cellular pathology; Pasteur, Koch and their confrères, into the land of bacteriology; Lister into the land of antiseptic surgery; Sajous and others into the fields of the internal secretions. But never in medical history has a larger or more varied domain been opened to pioneers than that of the x-ray by Roentgen. The discovery was unexampled in dramatic surprise and promise. It was like landing on a new continent where everything was different, incredible, transcending human experience.

The conquest of this new land was thus given to the hands of a fresh, eager generation of which Dr. Hickey became an outstanding figure. It is indeed a privilege given only to a few to live understandingly in the beginning days of a great discovery. Dr. Hickey was guided by unusual insight into the resources and fertility of this virgin soil. But the most enthusiastic predictions of the growth and development of the new rays fell far short of the realities to come. The miracle of shadows by invisible light gave increasing power and precision to diagnosis, and a new force, still unmastered, entered into the treatment of disease. The *Index Medicus* shows the astonishing rise of a vast literature but tells less than half because the roentgen rays form the leaven of innumerable articles under other titles in nearly every department of medicine, surgery and the allied sciences. However, the expansion, great and continuous as it was, never got beyond Hickey's grasp and he remained a leader to the end.

It is the part of the pioneer to brave dangers and hardship. In this far region of the spectrum were lurking unknown dangers, unseen, insidious, deadly. Many workers were maimed, some killed; others escaped by sheer luck. In those early days no one knew the strange power of those unfelt and invisible rays either to cure or destroy. America has her honored list of martyred dead. Dr. Hickey saw four of his most brilliant confrères and most valued friends, Caldwell, Leonard, Kassabian and Dodd, die lingering deaths. But once he had entered the way he never faltered. The persistence and daring of the pioneer were tempered in him by well-balanced caution. He was never injured and his reiterated advice taught uncounted friends as well as students to avoid the blighting effects of the new force which he helped to harness in efficient safety.

The influence of these new rays on human affairs proved vastly wider than the diagnosis and treatment of disease. Another source of x-rays was discovered in radium, for the gamma rays were found to be the rays of Roentgen. By their mutual help another splendid domain was opened in physics and chemistry, a domain glimpsed by Faraday, Maxwell and Helmholtz, who had to die before the promised land was entered. The exploration of the spectrum in the laboratory proved more thrilling than the exploration of equatorial Africa or the two poles. This led to revolutionary conceptions of the atom, of chemical affinities, of electricity, light, gravitation and energy, of the succession and transmutation of the elements and of the constitution of matter. Dr. Hickey delighted in the discussion of these problems and with his intimates enjoyed speculation and theory. Imagination has ever been the handmaid of research. Although in his own field a master of detail, practical, pragmatic, a respecter of ex-

perience, yet at large he was a philosopher whose vision and interests were far from limited by his daily routine.

He was always seeking the personal acquaintance of experimenters whose work had even a distant relation to the rays with which he had cast his lot. Pioneers in science like pioneers in a new country live often at isolating distances. It was an interesting characteristic in a man so little given to impulse, that he would go suddenly to some far point where he learned that new work was being done. These journeys ultimately included Europe and were the foundations of many enduring friendships.

Like Henry Adams his education was never finished and habits of close observation and study preserved an undiminished flexibility and vigorous mind. He had plans for books but was truly too busy to write them. He had visions of research but the network of daily duties held him prisoner. He covered an extraordinary industry under an easy-going manner and a youthful enthusiasm under a conservative exterior. Although his larger literary efforts had always to be postponed yet he wrote voluminously, his bibliography numbering 120 titles. While organized experimental work was largely denied him, nevertheless his daily work was for years a mine of clinical research, punctuated here and there by invention and discovery.

Dr. Hickey saw the rise of large industrial laboratories thoroughly equipped and endowed. Although the work was often altruistic and the workers unhampered, yet in his eyes there remained a traditional glory about the work of the individual genius in a lonely laboratory. The discovery of the x-ray is the finest example of pure science untouched by utilitarian motives. It was the culminating act of a long series of experiments, all of which seemed infinitely remote from human usefulness. The brilliant researches of a Crookes or a Lenard will not connect with the idea of patents and profits. Dr. Hickey debated the promotion of research without the sacrifice of the ideals of the pioneers. To his mind the answer was an endowed Chair of Experimental Roentgenology. It was after all a professor working in a college laboratory who discovered the x-rays.

Dr. Hickey belonged to many societies but always first in his affections, thoughts and efforts was the American Roentgen Ray Society. He adopted it in its precarious infancy and won fairly the affectionate nickname of Pa Hickey given him by old-time members. This Society he considered a necessary instrument for the stimulation of research and records in literary form, for harmony and coördination of workers over the land, for personal contacts and abiding friendships, for the development of a professional consciousness, for the enforcement of ethical standards and for a collective influence in the medical world. To forward these objects he undertook to publish the Transactions in the form of a quarterly magazine and thus founded the American Journal of Roentgenology, serving for years as its pioneer editor and manager. In those early days with a small membership within the Society and much indifference without, it became a personal struggle to keep the Journal alive. Every detail from printing to mailing, from soliciting subscriptions to facing a deficit was personally managed in his office by Dr. Hickey who at the same time had to make his living by the daily practice of his profession. When finally he relinquished the editorship he had placed the Journal among the few foremost publications of its kind in the world. It was a perfect example of successful pioneering by a man whose courage was so instinctive that he was unaware of it and whose vision was so clear that he thought others also must see.

He never knew the traditional loneliness of the pioneer. With a genius for friendship, companionable, tolerant, humorous, sympathetic, uncomplaining, with world-wide interests and information, always loyal, this kindly, patient teacher found his richest rewards in the affection of his students and of his contemporaries.

Carnegie is credited with the observation, "Pioneering don't pay." This, of course, depends on the kind of remuneration sought. To Preston M. Hickey pioneering paid in coin that can never depreciate and which has become the natural heritage of his fellow workers for all time. He died at the post of duty, still on the frontier, happy in planning new expeditions of discovery and devising methods for the best cultivation of lands already won.

May the Hickey Library to come continue to extend his helping hand to the earnest student and may this Plaque remain a sign foreover of the love and veneration of his fellows.

PRESENTATION OF BAS-RELIEF

By JOHN T. MURPHY, M.D.
President, Detroit Roentgen Ray Society

THE members of the American Roentgen Ray Society are pioneers in a new field of science. They have contributed much to the advancement of their special work. Not a little of this progress was the result of the untiring efforts of Dr. Preston M. Hickey.

We thank the University of Michigan because it was here that Dr. Hickey received his pre-medical training. It was this University that gave him the opportunity to fulfill his destiny as a teacher of young men.

Memories of Dr. Hickey are among the most prized possessions of the members of the American Roentgen Ray Society. These memories we share with you when we present this Plaque to the memory of Preston M. Hickey, Master Physician, Master Roentgenologist. May future men of Michigan, seeing this, be inspired to emulate his example.

ACCEPTANCE ON BEHALF OF THE FACULTY OF THE MEDICAL SCHOOL

By FREDERICK G. NOVY, M.D.
Chairman of the Faculty

I ESTEEM it a great privilege to accept, for and on behalf of the Medical Faculty, this splendid likeness of our late colleague, Dr. Hickey.

I wish to thank you, Dr. Murphy, for your felicitous words and I desire to convey through you to the American Roentgen Ray Society and to those whose efforts made this gift possible our appreciation of the motive in thus perpetuating his memory. The Medical School is proud in having had Dr. Hickey on its staff and is equally proud to possess this excellent bas-relief, a cherished memorial of a great and amiable man. I assure you that it will be given a worthy place amidst the activities in which he had a life-long interest. There, the presence of this plaque will keep alive the remembrance of the leading American pioneer in Roentgenology and will serve as a lasting stimulus to the young men who follow in his footsteps.

To me this tribute to Dr. Hickey is of special interest for I have known him for many years. Our acquaintance began while we were undergraduates in the Literary College. We sat together in the same classroom for a year and we often discussed matters of common interest and laid our plans for the future. His interest then was in languages, ancient and modern. It seemed at the time as if he were destined for a career in Greek. But the dreams of youth are subject to change.

Before long he took up the study of medicine and, after graduation, he found

his life-work in the diagnostic laboratory. The discovery of the x-ray by Roentgen in 1895 opened up for him a new field of activity. With the full ardor of youth he saw the great possibilities in this new science and it was there that he found the opportunity to develop his innate abilities. Through the subsequent years his keenness in observation, his solid judgment and his steadfast devotion to the scientific ideal brought him recognition at home and abroad, and, what is more, the unbounded admiration of his fellow-workers in Roentgenology. The presentation of this sculptured portrait is eloquent evidence of the high regard in which he was held.

He possessed a personality of rare charm and a lovable disposition which impressed those with whom he came in contact. He was genial and unruffled, quiet and unostentatious, sincere and true. Unselfish to a high degree, his helping hand was ever ready to give aid to those in need. Throughout his life he remained a student with a strong interest in the progress of science, in languages and literature, in art and music.

In honoring the memory of Dr. Hickey, we honor the scientist, the student, and the man among men.

ACCEPTANCE ON BEHALF OF THE UNIVERSITY

By ALEXANDER G. RUTHVEN
President, University of Michigan

AN OBSERVING poet has remarked, "When a great man dies, for years the light he leaves behind him lies on the path of men." Nowhere is this truth better exemplified than in the University—an institution with the principal objective of contributing to the material and spiritual welfare of man, an institution guided by idealists, an institution founded on faith in the value of education and conducted on the belief that knowledge is to be accumulated bit by bit.

The real university is a composite of the characters of staff, students and graduates. If faith is kept and the pursuit of knowledge conscientiously performed, it may be an edifice of usefulness and beauty reflecting the character of its great men as a beautiful building reflects the skill of the architect.

We, his colleagues and students, need no monument to the kindly spirit, faithfulness, and ability of Dr. Hickey for his memory will be perpetuated in our lives. For future generations of students, however, this portrait plaque should have the value of a visual reminder that here was a man to whom service was a joy and loyalty a common virtue. I accept this gift for the University, with a full appreciation of its value and of the affection which has led to its preparation and presentation.

GUIDO HOLZKNECHT
1872-1931

PROF. GUIDO HOLZKNECHT died in Vienna on the 30th of October, 1931, at the age of fifty-nine years. He was a great physician, a true scientist and a hero who was a martyr to his professional calling. There is no disciple of Roentgen to whom the name and accomplishments of Holzknecht are not well known and thousands of sick and injured have been benefited by his ministrations. Not very long after Roentgen's discovery, Holzknecht began to use the newly found weapon in fighting disease until finally his own body was ravaged and destroyed by the very agent he had applied so successfully to relieve others of their afflictions.

Holzknecht was a senior medical student when the x-rays were discovered and with keen foresight anticipated the tremendous rôle which the "all-penetrating rays" might play in medicine, and a few years later began to devote his entire time to the study of the science of roentgenology. He realized that the practice of this specialty would require familiarity not only with the underlying physical properties of the rays

and their mechanical and technical application but above all, a thorough understanding of normal and pathological anatomy and physiology from a clinical standpoint. It was on the basis of this logic that Holzknecht built the Vienna School of Roentgenology which attained such great renown.

Even in these early days we find great similarity in the methods of Holzknecht and Roentgen in their investigations. Both were experimenters and critically analytical of the problems which they attempted to solve and most conservative in the conclusions which they drew from their results. They both disliked verbosity and in their discussions with colleagues and students came quickly and clearly to the important points and carried on to logical conclusions. Over the door of Holzknecht's small office in the old Roentgen Institute of the "Allgemeine Krankenhaus" in Vienna hangs a German translation of the Latin proverb "Nemo fieri non posse" which may be translated into English to read "Nothing is impossible to anyone." Many interesting conferences took place under this proverb in this room where so many came to learn and profit from Holzknecht's vast experience.

When Holzknecht first became interested in the application of roentgen rays in medicine there were numerous startling reports about the marvelous therapeutic results which were obtained. However, he reasoned that by the empirical methods which were employed it would be an everlasting and impossible task to analyze the effects of the rays and that the only sound method would be that of measuring dosage so that it could be repeated and duplicated and that thus there would be a sound basis for determining therapeutic reactions. Therefore he studied the physical and chemical effects of the rays which might be used as indicators of the quantity and quality of the rays. He found a chemical substance which would change color under the influence of roentgen rays and on the basis of this color change he constructed his "chromo-radiometer" which was the first practical roentgen dosimeter. He described this method of measuring roentgen rays at the Second International Congress of Medical Electrology and Radiology, in September, 1902, in Berne, Switzerland. He presented four other papers on this important subject during the same year. There can be no doubt that the introduction of this dosimeter which was calibrated in Holzknecht units, or H, was a very decided advance in the development of radiation therapeutics. The Holzknecht radiometer is still used successfully in Vienna although other methods are also recognized and employed. Holzknecht was always actively interested in the development of roentgen therapy and particularly the improvements made in the methods of dosimetry. I recall with pleasure an enthusiastic letter which he wrote to me reporting upon his observations and satisfaction with one of the first "Mecapion" dosimeters which was based upon the ionization method. In October of this past year, just a short time before his death, in a very charming note he asked for a particular ionization dosimeter which is manufactured in this country so that he might make comparative studies of the merits of different types of dosimeters. It is remarkable that this pioneer in roentgenology retained such keen interest in roentgen technique and methods of dosimetry from his earliest work until the time of his death in spite of numerous other interests and onerous duties.

Holzknecht was a prolific writer and though he contributed much to the science of radiotherapeutics this was only a small part of his activities. In the first volume of Gocht's bibliography of the world's roentgen literature which appeared in 1911 and which lists the literature published from the time of the discovery of the roentgen rays until 1910, there were 114 papers and five books published by Holzknecht or in collaboration with his associates and these all within the first ten years of his experience with the roentgen rays. About 30

of these papers were devoted to radiotherapeutics and a like number to technical and physical subjects and the rest to roentgen diagnosis. Of course it is impossible in this short tribute to name the great number of literary contributions from the pen of this great scientist. In subsequent issues of Gocht's bibliography there are also listed 151 papers by Holzknecht and his coworkers which were published between 1911 and the time of his death so that the total number of his contributions to roentgen literature is well over 250 papers. This monumental collection presents a cross-section of all of the different branches of roentgenology and includes those on purely clinical subjects as well as others on technical and physical investigations and pedagogy.

As early as 1903 he published a booklet entitled "Die Radiologie als selbständiger Zweig der medizinischen Wissenschaft" (Radiology as an Independent Branch of Medical Science) in which he prophesied the present status of roentgenology as a specialty in medicine. Later in his life, Holzknecht renewed his interest in the status of the roentgenologist in addition to his other work and discussed the subject in many papers, an outstanding one of which is entitled "Status Roentgenologiae" which was translated into many languages and appeared in this country in *Radiology*. After discussing the important position which roentgenology had attained in association with all of the other branches of medicine and science and after commenting upon the development and improvements in the technique of roentgen procedures and apparatus he asked the question, "How are we to interpret and translate correctly all of the thousands of heterogeneous roentgenograms which are the product of roentgen apparatus and come to us in overwhelming quantity?" He answered this question by establishing two requirements —(1) sound basic foundation and education, and (2) division of labor and specialization. In order to carry out these ideals successfully, Holzknecht's own institute was subdivided into several departments and he delegated different problems to his coworkers and assistants. In addition to his roentgen laboratory he created an organization for the systematic training of physicians in radiology in all its branches and also a consultation service for professional colleagues of other specialties. He also established a research laboratory not only for clinical research but also for investigations in physics and the technical problems of industries. All of this was accomplished with a minimum of financial support from the government, the city or the hospital authorities. The impoverishment of the small Austrian republic after the World War rested heavily upon Holzknecht's institute and there was little money available for necessary improvements in the institution, but with splendid spirit the Director and his assistants continued their brilliant work with the generous support of some of the roentgen industries.

One of the outstanding accomplishments of Holzknecht in the field of roentgen diagnosis was his well-known publication entitled "Die roentgenologische Diagnostik der Erkrankungen der Brusteingeweide" (The Roentgen Diagnosis of Diseases of the Organs in the Chest) which was published in 1901 and was a remarkably complete treatise, especially when one considers the technical difficulties which existed in this early era of roentgenology. Holzknecht was one of the first to attempt to visualize the gastrointestinal tract with the roentgen ray by inflation with air or by means of opaque media. In January, 1906, he spoke before the Berlin Medical Society upon the diagnosis of the early stages of carcinoma of the stomach and its differentiation from ulcer. He was probably one of the first to recognize this diagnostic differentiation. It may be truly said from these and many other important contributions that Holzknecht was the "Father of Clinical Roentgenology."

Guido Holzknecht was born in Vienna on December 3, 1872, and was the son of a well-known manufacturer of that city. He

completed the courses at the Gymnasium in Vienna in 1891 and then studied medicine in Vienna and Strassburg with post graduate work in Berlin and Koenigsberg. In 1904 the Roentgen Institute at the "Allgemeine Krankenhaus" was established and shortly thereafter Holzknecht was made the Director and "Dozent for Radiology." In 1914 he was made Professor of Roentgenology when he was already very widely known. He was made an honorary member of many roentgen societies, among others the American Roentgen Ray Society. He founded and organized and was President of the International Association of College Teachers for Medical Roentgenology. During the World War he was commissioned Lieutenant Colonel and made the Chief Inspector of Roentgen Stations of the Austrian Army.

Holzknecht suffered serious burns of his hands from his early work in roentgenology. His right hand was particularly affected and a number of operations were necessary; however, the malignant processes progressed and his arm was eventually sacrificed. In spite of his affliction, Holzknecht was always optimistic. He designed an artificial arm for himself which he handled very skillfully. He continued his work in the institute uninterruptedly until he suffered from coronary thrombosis.

It may seem that Holzknecht's place as a master clinician and teacher cannot be filled; however he has left to the world many disciples who will continue his work and follow the ideals which he established in roentgenology.

Otto Glasser

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. E. P. Pendergrass, University Hospital, Philadelphia, Pa.
Thirty-third annual meeting: Detroit, Mich., 1932.

AMERICAN COLLEGE OF RADIOLOGY
Secretary, Dr. Albert Soiland, 1407 S. Hope St., Los Angeles, Calif.
Annual Meeting: New Orleans, La., 1932.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. G. W. Grier, Jenkins Arcade, Pittsburgh, Pa.
Annual meeting: New Orleans, La., May 9–13, 1932.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. I. S. Trostler, 812 Marshall Field Annex, Chicago, Ill.
Eighteenth annual session: To be announced.

RADIOLOGICAL SECTION, LOS ANGELES COUNTY MEDICAL SOCIETY
Secretary, Dr. John F. Chapman, 209 Professional Bldg., Pasadena, Calif.
Meets on the third Wednesday of each month at the California Hospital.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. W. S. Lawrence, Medical Arts Bldg., Memphis, Tenn.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. J. J. Masterson, 401–76th St., Brooklyn, N. Y.
Meets monthly on first Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N.Y.
Meets second Monday of each month except during summer months, place of meeting selected by the host.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. George M. Landau, 660 Groveland Park.
Meeting second Thursday of each month October to May inclusive at Virginia Hotel.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. A Srauss, 518 Medical Arts Bldg.
Meetings are held at 6:15 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. E. R. Witwer, Harper Hospital.
Meets monthly on first Thursday from October to May, at Wayne Country Medical Society Building.

FLORIDA RADIOLOGICAL SOCIETY
Secretary, Dr. F. K. Herpel, Good Samaritan Hospital, West Palm Beach, Fla.
Meetings held twice a year, May and November.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Fauntleroy Flinn, 220 South Webster St., Decatur, Ill.
Regular meetings held quarterly.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. J. N. Collins, Indianapolis, Ind.
Annual meeting each February 22 in Indianapolis.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. J. E. Habbe, 221 Wisconsin Ave., Milwaukee, Wis.
Meets first Friday in October, December, February and April.
Place of meeting designated by the president.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. L. G. Rigler, University Hospital, Minneapolis, Minn.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. Thomas R. Healy, 370 Marlboro St., Boston, Mass.
Meets monthly on third Friday, Boston Medical Library.

NEW YORK SOCIETY
Secretary, Dr. J. Bennett Edwards, Englewood Hospital Englewood, N. J.
Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. R. C. Hall, 258 Genesee St., Utica, N. Y.
Three meetings a year—January, May and November.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. W. E. Reiley, Clearfield, Penna.
Next meeting, to be announced.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. Karl Kornblum, 3400 Spruce St.
Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thomson Hall, College of Physicians, 19 S. 22d St.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Camp C. Thomas, 476 Lake Ave.
Meets monthly on the first Friday evening at 7:45 at the Rochester Medical Association Building.

ST. LOUIS ROENTGEN CLUB
Secretary-Treasurer, Dr. E. W. Spinzig, 316 Metropolitan Bldg.
Meets first week of each month. Time and place of meetings designated by president.

TEXAS RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. C. P. Harris, Houston, Texas.
Meets annually one day preceding the meeting of the Texas State Medical Association.

UNIVERSITY OF MICHIGAN ROENTGEN RAY SOCIETY
Secretary, Dr. C. C. Taylor, University Hospital, Ann Arbor, Mich.
Meets first and third Wednesday evening of the month from October to June, at 8 o'clock in the amphitheatre of the University Hospital.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Virginia Roentgen Ray Club
Secretary, Dr. Wright Clarkson, 205 S. Sycamore St., Petersburgh, Va.
Next meeting, to be announced.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 p.m., at 32 Welbeck St., London, W. 1., or as advertised.

Electro-Therapeutic Section of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:30 p.m. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Colin Macdonald, Lister House, 61 Collins St., Melbourne, Australia.
Meets monthly at Melbourne during the winter.

Section on Radiology, Canadian Medical Association
Secretary, Dr. A. H. Rolph, 160 St. George St., Toronto, Ont.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. P. C. Fenwick, The Hospital, Christchurch. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Allies, 134, Louvain (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Societe de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11/52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd-und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Roentgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the Fall.

Societa Italiana Radiologia Medica
Secretary, Professor M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Nicolae Busila, 44 Elizabeta Blvd., Bucarest.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson.
Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan. Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology of Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Society of Roentgenology
Secretary, Professor Holzknecht, Vienna, IX, General Hospital.
Meets first Tuesday each month, October to July.

Orient

Japan X-ray Association
c/o Orthopedic Surgery, Tokyo Imperial University.
Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto, Japan. Meets bi-monthly on third Sunday.

FLORIDA RADIOLOGICAL SOCIETY

The Florida Radiological Society, composed of radiologists practising in the State of Florida, was formally organized on November 14, 1931, at St. Petersburg, under the temporary chairmanship of Dr. L. W. Cunningham of Jacksonville. A Constitution and By-laws were adopted at this organization meeting, and the following officers elected to hold office until the Spring meeting in 1932: President: Lester W. Cunningham, M.D., Jacksonville; Vice-President: Orion O. Feaster, M.D., St. Petersburg; Secretary-Treasurer: Frederick K. Herpel, M.D., Good Samaritan Hospital, West Palm Beach, Florida.

Meetings will be held twice each year, November and May, the latter meeting being held the day before the annual meeting of the Florida State Medical Association.

The radiologists of Florida have been meeting informally twice each year for several years, and the permanent organization only cements an already existing series of contacts between and among those physicians practising radiology in Florida.

FREDERICK K. HERPEL
Secretary

OWNERSHIP OF ROENTGENOGRAMS

The question whether the roentgenograms of a hospital patient belong to the patient or to the hospital was answered by a court for the first time, so far as is known, in *Hurley Hospital* v. *Gage*, decided on appeal, April 21, by the circuit court for the county of Genesee, Mich. The patient had been roentgenographed in the roentgenographic department of the Hurley Hospital at Flint. The usual charge for the service was included in the patient's bill. He made a payment on account but refused to pay the charge for roentgenographic service unless the roentgenograms were delivered to him. The hospital refused to deliver them and sued the patient for the balance due. In the justice's court where the suit was instituted, judgment was given against the hospital. The hospital, however, because of the principle involved, appealed to the circuit court of Genesee County. At the hearing on the appeal, no one appeared on behalf of the patient and the case was heard and judgment rendered without the submission of evidence or argument by him. In giving judgment, the court pointed out that the hospital sold and patients paid for, not the material that went into roentgenograms, but knowledge and experience. The protection of the hospital might depend largely on the proper preservation of the roentgenograms and, said the court, the films should remain with the hospital. Judgment was given against the patient for the balance due on his bill, covering the amount charged by the hospital for the roentgenograms.—*Jour. A. M. A.*, Nov. 21, 1931.

BOOK REVIEWS

Books Received Are Acknowledged under Heading: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers as space permits.

Causation, Diagnosis, and Treatment of Cancer. By James Ewing, M.D. The Beaumont Foundation Lectures, Series No. 10. Published by the Williams & Wilkins Co., Baltimore, for The Wayne County Medical Society, Detroit, Michigan.

It is scarcely compatible with sound criticism for this book to be reviewed by anyone who sat under the spell of the distinguished author as he delivered these lectures. For Ewing has attained that level of science where the scientist is an artist; and those who heard these lectures felt this as surely as if they hung on a Shakespearean's lines or listened for the oboe's echo. But after some months the book appears and the printed page recreates the fine thrill of a superb performance. One need read only a few pages to sense that here is vast erudition, sanity, clarity, and order—and a facility of expression which constantly amazes.

At the outset of his discussion of causation of cancer the author clears away a great heap of mental rubbish. He first explains in a very lucid and convincing way the necessary distinction between the exciting factors in the disease and the nature of the disease process. His next step is effective disposal of the unsupported belief that cancer is an infectious process, presumably to be understood and controlled by discovery of a germ. His final introductory touch is a critical examination of the convenient but erroneous assumption that cancer is a single disease.

Having defined his problem the author then takes up a review of present knowledge of cancer causation. The scope of the Cohnheim theory is measured, the theory of tissue tension is exhibited, hereditary influence is tentatively weighed, and animal parasites are studied as an exciting factor. Roentgen rays, aniline products, growth-stimulating substances and chemical studies are discussed. The clinical causes of many forms of cancer are stated to be "very well known in many cases, and fairly well surmised in many others."

The lecture on diagnosis is opened with the statement that "the keystone of cancer control is early and accurate diagnosis." The difficulty, as well as the importance, of early diagnosis is stressed. "The suspicion of cancer should be constantly in the mind of the alert physician, for only thus can he pick up the early cases. The prediction of cancer, and if possible its prevention, should be a constant responsibility in the mind of every practicing physician." The "attitude of innocence and unpreparedness with which the average physician approaches the diagnosis of cancer" is attributed to a popular notion that "cancer is cancer, much the same at all times and places," and to "the utterly inadequate opportunity for medical students and graduate physicians to see cancer in sufficient number and detail to give them adequate information about it." Though histologic study is given as essential to complete diagnostic information, physical examination is stressed as covering the largest field, and as being responsible for discovery of the majority of malignant tumors. This discussion is most important, and for practical considerations is perhaps the high spot of the book.

The perennial problem of biopsies is discussed at length. Although favoring a biopsy when planning a major operation or extensive irradiation, the author deplores the fact that the easy resort to biopsy may lead to neglect of other less serious methods of obtaining information. The method of taking tissue specimens is considered. Caution is urged in removal of lymph nodes for diagnosis. The difficulties in histologic diagnosis are recognized. Grading as to radiosensitivity and malignancy is revealed as placing a heavy responsibility on the pathologist, requiring him to acquire broad knowledge of the entire subject of tumors and their treatment.

The subject of treatment is discussed in general, surgery and radiation being weighed as to their respective merits and proper scope. The treatment problems presented by specific forms of cancer are then taken up in more detail. In general the author accords radiation a somewhat broader field than it has so far won among most other cancer authorities. Before closing his final chapter the author pauses to deplore the abundance of fantastic cancer remedies and their patronage among persons who have never

received (and others who have never comprehended) medical education.

The serious student of cancer or the casual reader will find this book absorbing reading. Written in exceptionally lucid and graceful style, it presents a succinct summary of present-day knowledge and expresses the deliberate opinions of one of the most profound students of this great problem.

C. E. Dutchess

Radiologie medicala (notiuni pregatitoare si technica generala). (Medical radiology: Fundamental Principles and General Technique.) By Dr. Dimitrie Negru, Professor of the Medical Faculty of Cluj, Rumania. Paper. Price, 380 Lei. Pp. 470, with 263 illustrations in the text. Cluj: Tipografia "Cartea Românească," 1931.

Professor Clark, of the University of Illinois, in reviewing in a recent article (see this Journal, October, 1931, *26*, 528–539) the contributions of a quarter century of electron physics to roentgen-ray science, made the following unequivocal statement concerning the complexity and remarkable mechanisms of the problems confronting the roentgenologist in his daily work: "Every single treatment, every moment of operation of apparatus, every physical, chemical and biological effect involves the fundamental principles of electron physics which are still imperfectly known. Upon a knowledge of these principles, the progress of roentgen-ray science has depended and must depend for correct design of equipment, correct dosage and the greatest measure of effectiveness in promoting human welfare." Through a happy coincidence, the author of the book under review prompted, no doubt, by a similar line of thought makes electron physics the basis of his treatise. Thus he commences with the electron and by closely following its behavior under various circumstances, deducts all the fundamental laws of electricity from the phenomena caused by its perturbation. Under the everlasting influence of this negatively charged particle of the physical universe, he takes the reader step by step through the vast fields of static electricity, magnetism, electromagnetic vibrations, electrochemical phenomena, electric discharges in rarefied gases, theory of relativity of Einstein, Bohr electron theory of the structure of the atom and its more recent displacement by the quanta and wave mechanics, to arrive at the intricate problems of radiation emission, physical and chemical properties of the roentgen rays, absorption phenomena and finally the construction of tubes and apparatus. In the last part of the book the general principles of roentgen diagnosis (roentgenoscopy and roentgenography) and of radiation therapy (both roentgen and radium therapy) are briefly discussed. In connection with these, the author describes several of his own methods such as the method for the localization of foreign bodies with the aid of the roentgenoscope, the procedure for the determination of the angle of obliquity of the body as compared to the screen in the various oblique positions of roentgenoscopy of the heart, the so-called "oval diaphragm" which is used advantageously in the treatment of uterine carcinomas, etc.

As a whole, the book is written in a simple, concise manner with omission, even in the highly abstract domains as much as is compatible with the clear expression of the ideas, of the intricate mathematical formulae or too sophisticated theoretical argumentations. For the sake of convenience and since the purpose of the book is primarily didactic, the various subjects are treated in separate chapters arranged numerically (271 altogether). The intention of the author, as he himself states in the preface, is "that the known facts form a sort of museum permitting the student by walking through its orderly arranged rooms to instruct himself in a progressive and systematic manner." Yet this museum-like arrangement does not constitute simply an enumeration or tabulation of the physical facts and laws, for the author has always essayed to co-ordinate physical phenomena and their rules with biologic observations, bearing in mind that the roentgenologist is in the first instance a physician, whether he studies radiation energy in its relation to matter or applies it in the art of healing.

T. Leucutia

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

HEAD

Illig, Werner. Über die Dauer der Sichtbarkeit von kindlichen Schädelfrakturen im Röntgenbild. (On the duration of the roentgen visibility of skull fractures in children.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Jan., 1931, *43*, 76–85.

Stewart, who made a detailed study of fractures of the skull, arrived at the following conclusions with regard to the duration of the roentgen visibility of the fracture lines: a simple linear fracture disappears in children within six to eight months, while in adults the fracture line may persist for three years or longer; the fractures in the occipital region, because of the thickness of the bone, heal more slowly both in adults and children, and the depression fractures, with displacement of the fragments, often lead to permanent defects, in all instances the individual variation being of paramount importance.

The author, analyzing his cases from the standpoint of the above findings, was able to confirm Stewart's conclusions, especially as regards the healing of fractures of the skull in children. Thus it was found that even severe depression fractures with bone defects heal completely so that a roentgen examination of the skull within four to five months may be entirely negative.

It is important that roentgenograms of the skull in children be made as soon as possible following the slightest trauma. The visualization of linear fractures in apparently symptomless cases will often aid in the later demonstration of the cause of traumatic epilepsy.

Sixteen cases are briefly described, several of them being illustrated with roentgenograms.—*T. Leucutia.*

Castronovo, Ettore. Sulla craniostenosi familiare ereditaria-disostosi cranio-facciale. (Hereditary familial craniostenosis—craniofacial dysostosis.) *Radiol. med.*, Mar., 1931, *18*, 325–346.

The author describes a family with hereditary familial craniostenosis. The mother had always had moderate exophthalmos and marked prognathism with eyes very far apart. She had no disturbance of vision; she had good health except that up to the age of twenty she had rather intense attacks of headache. There was no history of a similar condition in her family. Her husband was normal. She had two normal children and then four with the same anomalies that she had—exophthalmos, small, hooked nose and prognathism. They also had varying degrees of disturbance of vision.

He thinks this case was one of Crouzon's type of craniofacial dysostosis. He compares the anatomical and roentgen pictures of this hereditary familial form with those of a typical case of sporadic oxycephalic craniostenosis. He reviews the different forms of craniostenosis described in the literature and makes a differentiation between false forms and primary natural synostoses. He proposes a classification for the latter based on the results of anatomical and roentgen examination. He agrees with Bertolotti that Crouzon's craniofacial dysostosis is not an independent disease but only one of the group of primary craniostenoses. He discusses the optical lesions and their relation to the roentgen picture of intracranial hypertension, which is probably less than it appears to be. The exophthalmos is not at all like that of Basedow's disease. He studied the optical canals, the sella turcica, the spheno-basilar synchondrosis and the sinuses and gives illustrative roentgenograms. While he reserves judgment as to the pathogenesis of craniostenosis he thinks that the hereditary and familial form argues against the meningitic nature of the disease and shows that it is idiopathic.—*Audrey G. Morgan.*

Meagher, Richard, and Eisenhardt, Louise. Intracranial carcinomatous metastases; with note on relation of carcinoma and tubercle. *Ann. Surg.*, Jan., 1931, *93*, 132–140.

The authors present statistics on a series of 1,850 verified intracranial tumors. Of this number 57 are metastatic, 44 of which are carcinomas, 9 are sarcomas and 4 are hypernephromas. Of the metastatic tumors 60 per cent are secondary to lesions in the breast and lung.

The writers stress the fact that from a diagnostic point of view the so-called typical his-

tory of a very rapid progress of an intracranial lesion, often with accompanying psychosis, cannot always be relied upon, even in cases of established breast cancer. They cite two cases of intracranial lesions in patients with proved breast cancer, one of which was a meningioma and the other, in a patient with disseminated tuberculosis, proved to be an adhesive tuberculous meningitis plus metastatic malignancy from the breast.

The recent revival of interest in the possibility that carcinoma and tuberculosis are antagonistic diseases is not subscribed to by the authors. They review much of the literature relative to this controversy.—*F. K. Alexander.*

NECK AND CHEST

MELLER, OSKAR. Beitrag zur Kenntnis der Lymphgefässe der Lunge—eine anatomisch-röntgenologische Studie. (Contribution to the knowledge of lymph vessels of the lung—an anatomico-roentgenologic study.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Jan., 1931, *43*, 66–71.

The knowledge of the anatomic distribution of the deep lymph vessels of the lung is as yet incomplete. After numerous experiments in association with Menkes, the author found that thorium-hydroxidhydrosol (a preparation known as "umbrathor") can be advantageously used for the roentgen visualization of the pulmonary lymphatic system. Fresh lung specimens of adults were employed for the purpose of experimentation, the injections being made according to the method of Bartels, either directly into the lymphatic vessels or interstitially into the lung parenchyma.

Good roentgenograms were obtained showing a rather uniform distribution of the injected substance within the lymph vessels. As is known, umbrathor is a hydrophobic colloid which flocculates when in actual contact with catalases. Since the lymph stream is rich in such catalases, within a few seconds a rather uniform precipitation of the umbrathor results, leading to good roentgen visualization. The investigations will be continued.—*T. Leucutia.*

COLE, L. G., MORSE, R. W., POUND, R. E., HEADLAND, C. I., and COLE, W. C. The site of predilection in cross-infection from the right to the left lung. *Radiology*, Dec., 1930, *15*, 627–636.

Infections of the right lung which result in destruction of pulmonary tissue not infrequently give rise to infection in the opposite lung. This is termed "cross-infection" by the authors. They consider it an autogenous infection due apparently to the inhalation of infectious exudate and detritus. Although cross-infection of this type may occur in any part of the left lung, there is such a tendency for it to occur in a region midway between the apex and base that this can be considered the site of predilection. In roentgenograms made in the usual posteroanterior projection this area lies between the second and fifth ribs. The entire area may be involved but usually the focus, if early, will be limited. When a destructive lesion involves particularly the right upper lobe one would expect aspiration infection of the right lower lobe to precede cross-infection, for the bronchus to the right lower lobe is an almost direct continuation of the trachea. This type of secondary infection does occur, usually in association with cross-infection, but is most often limited to the peribronchial tissues. In certain cases, however, secondary infection of the lower lobe is more extensive than the cross-infection. The authors present numerous roentgenograms illustrative of cross-infection in tuberculosis and bronchopneumonia.—*J. D. Camp.*

FISCHEL, KARL. Nonapical infiltrations in pulmonary tuberculosis. *Am. Rev. Tuberc.*, Feb., 1931, *23*, 139–168.

Redeker and his followers, while not denying the possibilities of phthisical development from apical tuberculosis, claim that the significance of apical lesions as a forerunner of progressive disease has been grossly overestimated. The fact that changes in other parts of the lungs seem to be almost invariably preceded by positive findings at the apices, likewise innumerable necropsy reports revealing pathological processes apparently of longstanding in the apical region, whenever tuberculosis involving other parts of the respiratory organ was present, and even in the absence of a history of active tuberculosis during life, seem to prove conclusively that the apices were the site of predilection from which pulmonary tuberculosis first develops and begins its disastrous course toward the base.

The traditional physical and roentgen findings are easily explained by the fact that any lesion in the subclavicular region will tend to diminish the elasticity of the lung above, and that scar formation may often interfere with proper aeration of the apices.

The object of this article is to show that the German school emphatically rejects the slow evolution and gradual extension from involvement of the apical field. They contend that pulmonary tuberculosis nearly always begins with a bronchopneumonic focus in some part of the lung below the clavicle, from which it spreads by the formation of new foci to the middle field and the base, involving the apices at a much later period.

In a study of 117 cases of early infiltrates Redeker reported the localization as being infraclavicular in 38 cases, middle field in 38, lower field in 15, subclavicular in 4 and apical in 2.

The author presents statistical data and clinical observations to support the above views.—*F. K. Alexander.*

Frothingham, Channing. The differential diagnosis between pulmonary tuberculosis and pulmonary or bronchial malignant neoplasms. *Am. Rev. Tuberc.*, Feb., 1931, *23*, 107–119.

An accurate diagnosis is always desired, and this is especially true in cases in which the diagnosis may be confused between two conditions as in the title, which call for quite different procedures in regard to treatment.

A review of the symptoms presented by the 39 cases studied convinced the author of the fact that there is no outstanding initial symptom or character of onset which would justify one in more than suspecting primary malignant growth in the bronchus or lung from the history of the case alone.

Physical examination gives findings which depend upon the size and position of the growth. A large lesion gives evidence of an infiltrated or consolidated area in some part of the lung. If there is obstruction to the main bronchus by the growth the signs of mediastinal displacement will be in evidence. This displacement is always towards the side of the tumor and it is very unusual for a tumor to displace the heart and mediastinum away from the side of the tumor in the manner that a pleural effusion does.

Clinical laboratory findings are of very little help in making a differential diagnosis.

Examination of the chest by the roentgen ray gives the best method of procedure for the correct differentiation of the conditions under discussion. The roentgenograms of the lungs in these cases vary markedly in relation to the size and location of the growth and the correct interpretation is often exceedingly difficult. A comparison of films taken after a moderate interval may help to clear up the diagnosis in doubtful cases and a therapeutic dose of roentgen radiation is sometimes helpful. The bronchoscope gives a medium through which it is possible to actually see many of the tumors, especially those which show up least in the roentgenogram and in addition it may be possible to obtain a bit of tissue for microscopic examination.

The correlation of physical findings, the repeated study by the roentgen ray, supplemented by the use of the bronchoscope when adaptable, will usually reveal information which will make a differential diagnosis possible and enable one to institute the proper therapeutic measures indicated.—*F. K. Alexander.*

Reilly, William A., and Bolin, Zera E. Acute generalized tuberculosis without typical tubercles. *Am. J. Dis. Child.*, March, 1931, *41*, 582–590.

The authors present a case in which generalized tuberculosis assumed an unusual form. The blood stream infection in their patient was followed by lesions showing few mononuclear cells, no giant cells, few lymphocytes and large numbers of polymorphonuclear cells, with great numbers of tubercle bacilli in each lesion. Their explanation offered for this type of lesion is the large number of bacilli present, coupled with the nonresistance and lack of allergy of the patient. The course of the disease was about as follows: An infection by a large number of bacilli was present, probably acquired from the grandmother, which caused a large caseous lesion in the right upper lobe. The regional lymph nodes were involved from this lesion, and at the same time or later, bacilli entered the blood stream by the way of the lymphatics and thoracic duct, and caused nodular lesions in the lungs. Following the formation of these lesions, the bacilli spread by the blood stream to the general circulation and seeded the other organs of the body, and caused a lesion on the skin of the buttocks. Theoretically, the evolution of the process occupied about eight weeks. From this time there must have been rapid local multiplication of the bacilli in each area. They regard this as probable because of the great number of organisms seen in each lesion. A roentgenogram of the chest showed a process suggestive of miliary tuberculosis.—*R. S. Bromer.*

AIRALE, GIOVANNI. Echinococcosi pulmonare diffusa secondaria. (Secondary diffuse pulmonary echinococcosis.) *Arch. di radiol.*, Jan–Feb., 1931, *7*, 51–55.

Devè experimentally demonstrated in animals the appearance of secondary echinococcus cysts following the injection into the trachea of echinococcic fluid taken from humans. This proves that the echinococcus may be disseminated by the bronchial route. A second form of dissemination is by the blood stream.

Two cases of echinococcus cysts of the lungs are briefly described, the first failing to produce dissemination even after a long period, the second having resulted in secondary involvement of both lungs following spontaneous rupture of a primary echinococcus in the region of the hilus. There can be no doubt that in this second case the dissemination was by the bronchial route.—*T. Leucutia.*

CARR, WALTER LESTER. Observations on the thymus. *Arch. Pediat.*, March, 1931, *48*, 202–205.

Carr's paper is based on records made at the various hospitals with which he is connected and from statistical information available in the Department of Health and the Medical Examiner's Office of New York. He first quotes the weight of the thymus as given by various previous writers and then gives the results of the study of two groups of cases examined roentgenographically by himself. Anteroposterior and posteroanterior views were employed. He makes no mention of the use of the lateral position, In the first group of cases he states that the average transverse width of the thymus was 2.7 cm. and in the second group was 3.1 cm. as measured at the level of the third dorsal vertebra.

From his study of the records of the Medical Examiner's Office he concludes that children who have thymic conditions causing death are not the infants observed in a maternity hospital but children of an average age of five to six years at the period when operations for tonsils and adenoids are most required. It must be decided whether babies who have roentgen films made at the time of birth show anything of value compared with the films made in later childhood. In the latter group it is absolutely essential that a physical study should be made of the patient before operation as a roentgen record adds to a more thorough knowledge of the patient and is also a safeguard against a criticism of neglect. It is his opinion that an anesthetic properly administered by a competent anesthetist minimizes the danger from what is designated as a thymic death.—*R. S. Bromer.*

RABINOWITSCH, A. M. Zur Diagnostik der Thymome. (On the diagnosis of thymoma.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Jan., 1931, *43*, 71–75.

A case of thymoma with metastases to the lungs which was observed in a man forty-nine years of age is briefly described and illustrated with roentgenograms showing the progress of the lesion.

In discussing the criteria of differential diagnosis, the conclusion is reached that roentgen examination of the chest permits only a probable diagnosis.—*T. Leucutia.*

STEIN, ARTHUR, and TOREK, FRANZ. Adenoacanthoma of the uterus with metastasis to the posterior mediastinum and lungs. *Surg., Gynec. & Obst.*, Dec., 1930, *51*, 856–862.

An adenoacanthoma is a combination of cylindrical tumor cells and squamous cells, the latter probably developing from the former, although the histogenesis is rather uncertain.

The author reviews the literature and the article contains a rather complete bibliography. A case is reported which developed a mediastinal metastasis thirty months after hysterectomy. The mediastinal tumor was removed surgically and the case terminated fatally. No radiation therapy was employed.—*J. H. Vastine.*

HOSOI, KIYOSKI, and STEWART, F. CONSTANCE. Differential diagnosis of mediastinal "tumors." *Arch. Int. Med.*, Feb., 1931, *47*, 230–258.

On the basis of a study of 8 cases of different types of mediastinal tumor masses which they report, the authors conclude that there is not a single pathognomonic symptom or sign on which one can place absolute trust in the differential diagnosis of mediastinal tumors. Metastasis to the central nervous system is commonly observed. Such metastasis may initiate and dominate the symptomatology. Hence, a diagnosis of primary tumor of the brain may be made in these instances.

The suspicion of tuberculosis may be the diagnosis in the early stages for the physical

signs, together with the cough due to bronchial irritation from the growing tumor mass, may be a prominent symptom.

Clinical observations must be correlated with the roentgen and laboratory data. Confirmatory evidence is obtained by examination of the sputum or pleural fluid for tumor cells, examination of the specimen obtained by probatory puncture or through the bronchoscope, and examination of the superficial lymph nodes containing the metastases via biopsy.—*F. K. Alexander.*

Cherry, Homer H. Tuberculosis among children. *Arch. Pediat.*, Jan., 1931, *48*, 16–30.

Literal interpretation of the term juvenile tuberculosis, according to Cherry, should be all tuberculous infection involving the lungs and immediately related structures of children. He believes that tuberculosis in children may be classified using anatomical distribution, roentgen characteristics and clinical findings to develop this classification. Latent cases occur in large numbers and tuberculosis as found in children, is actually largely latent. This is the result of two factors: first, the early lesions are closely associated with the lymphatic system; second, the tissue of children, chiefly the lymphatic tissue, is capable of more swift and vigorous reaction than tissue of adults. He suggests the following classification:

Childhood tuberculosis.
A. Latent tuberculosis.
  (1) Tuberculous infection.
  (2) Pulmonary.
  (3) Hilum.
  (4) Hilo-nodular.
  (5) Apical.
B. Active tuberculosis.
  (1) Hilum.
  (2) Pulmonary.

The existence of the tubercle bacillus cannot be detected in the pre-allergic tissue, since the field of offense against the bacillus is microscopic in size, hence physical and roentgen means can only detect tuberculous infection after allergy sets in. The roentgen ray is required to demonstrate the existence of hilo-nodular tuberculosis (Ranke's complex), which comprises that vast group of cases represented by a primary tubercle, densely fibrous or calcified, with or without a fibrous band leading to the hilum where calcified glands are present.

Active hilum disease in children takes the form of lymphatic tuberculosis. The presence of roentgenological evidence depends entirely on extent and duration. Active tuberculosis in children, especially infants with breaking down of lung tissue, is usually fatal. It is necessary for hilum shadows in the roentgenogram to be fairly extensive to produce roentgen changes. The whole mediastinal space may show widening and nodulation. Occasionally single glands can be seen protruding into the medial surface of the lung. When calcium is present these glands are likely to be inactive. It is not unusual to see calcified glands on one side and caseous glands on the other, or both on the same side. The roentgen and physical findings in widespread active childhood tuberculosis are those of adult tuberculosis. In some cases, however, the outcome is not fatal, the systemic reaction, although profound at the onset, rapidly abates so that at the end of three to five weeks or even one week, the normal plane is again reached and the child seems to have suffered no consequence. Upon roentgen examination there will be found a uniform opacity in one lung field. The upper lobes are usually the site and there is meager evidence of tubercle formation. Clearing is slow. Four months to two years later the end-result is a few small deposits of calcium which have slowly arisen from cellular confusion. Well-kept infants below seven years of age are most likely to show this sequence of events.

Summing up diagnostic signs in general, Cherry states that neither roentgen or physical examination should dominate. Of the two, the roentgen examination is the more important. Good stereo films will enable one to detect minimal amounts of disease which otherwise would go undetected. In the supervision of patients, the roentgen film is essential because it gives warning of a dangerous hilum, small increases of parenchymatous infiltration, and furnishes the best estimate when the patient is safe to go on normal routine.

He regards a skin test as not an indication of disease when positive, but only as indicative of allergy. Latent pulmonary lesions offer fair prognosis; latent hilum lesions offer good prognosis. Calcification or complete absorption of fibrous deposits adds materially to a favorable outlook. Treatment of certain cases is absolutely indicated and is essential to good recovery. Basal changes are very infrequently tuberculous.—*R. S. Bromer.*

KOHN, JEROME L., and KOIRANSKY, HENRY. Roentgenographic reexamination of the chests of children from six to ten months after measles. *Am. J. Dis. Child.*, March, 1931, *41*, 500–506.

In a previous paper, the authors reported the observations on successive roentgenograms of the chests of 130 children taken during measles. It was shown that shadows suggesting pulmonic infiltrations were present in 62.4 per cent of the patients less than four years of age and in 42.2 per cent of the patients four years of age or over. In the cases showing infiltration, this was present in at least 61 per cent before or during the height of the eruption. Thus the infiltration was often present in cases which were considered clinically mild. Abnormal intensity of the pulmonary markings, pleuropulmonary changes and progressive and retrogressive hilar changes were also present.

The purpose of the present paper is to report the observations on roentgenographic reexamination of the chests of these children from six to ten months after measles. Fifty-six of the patients previously studied returned for the re-examination. Unfortunately no roentgen examinations before the onset of measles were possible. The roentgen technique was the same in both series of examinations. In the roentgenograms of the chests of the children re-examined, changes were noted (1) at the site of a previous pulmonary infiltration, (2) at the site of a previous abnormal intensity of the pulmonary markings, (3) in the pleura and (4) in the hilar shadows.

It was found that previous pneumonic infiltrations, even when extensive and of long duration, showed few or no pulmonary changes on roentgen re-examination. These changes, when present, were described as localized accentuation of the pulmonary markings. It would seem that if the child recovers from a severe case of measles, complicated by extensive pulmonary involvement, the chances of residual changes in the lungs such as chronic fibrosis or bronchiectases, are slight.

Abnormal intensity of the lung markings was present during measles in 80 per cent of all cases in the authors' first study. On return, only 4 children showed these abnormal markings and they were only present to a slight degree.

The evidence of pleural involvement during measles was striking. In 18 cases pleural thickening not seen on the roentgenogram during measles, was present on re-examination. From their cases, Kohn and Koiransky conclude that changes in the pleura as the result of measles appear to be frequent.

On cases re-examined the density of the hilar shadows had diminished when compared with roentgenograms taken during measles. The interval history showed that after discharge from the hospital most of the children had remained well. Physical examination of the lungs gave normal results even in patients who had been severely ill with extensive pulmonary and pleural involvement while in the hospital.—*R. S. Bromer.*

HIRSCHBOECK, FRANK J. Spontaneous pneumothorax. *Ann. Int. Med.*, Jan., 1931, *4*, 705–722.

By spontaneous pneumothorax the author means all pneumothoraces which are not induced by external factors, either accidental or for therapeutic purposes.

The condition occurs most often between the ages of fifteen and forty-five years. Males are affected more often than females, in the proportion of 4 to 1. It occurs with equal frequency on both sides of the chest. It may be multilocular or unilocular, depending on pleural limitation; partial or total; unilateral or bilateral; simple or complicated by effusion, and may be recurrent.

The pneumothoracic cavity may be of the closed type, meaning a sealing up of the communication between the pleural cavity and the pulmonary tissue; open, if a free communication exists between the pleura and the pulmonary fistula; or of the valvular type if a check-valve action is developed.

Pulmonary tuberculosis is the most frequent cause of spontaneous pneumothorax. Beach in his series of 918 cases stated that 77 per cent were tuberculous in origion. Rose believes the percentage is 80 while Gerhardt considers it to be as high as 90 per cent. Other etiological factors which have been considered are pneumonia, pleurisy and rupturing of an emphysematous bleb. The author holds that the latter condition is the most common of the non-tuberculous etiological factors.—*F. K. Alexander.*

ABDOMEN

TARTAGLI, DINO. La morfologia duodenale sotto il rispetto anatomo-radiologico. (The

morphology of the duodenum as shown by anatomical and roentgen examination.) *Radiol. med.*, Mar., 1931, *18*, 289–308.

The pictures of the duodenum shown by roentgen examination differ in some respects from those described in the classical textbooks of anatomy. The roentgen pictures show U-shaped, V-shaped and semicircular duodenums, and only the U-shaped ones show the characteristic transverse and ascending portions described by the anatomists. The author studied the bulb of the duodenum in 40 subjects and tried to establish a relationship between its size and shape and the various types of constitution. The general form of the bulb is triangular in all types of constitution. This seems to be due to the ligaments and the position of the duodenum with relation to the stomach. Variations in the form are caused by changes in the tonus of the walls and the pressure of neighboring organs. The site of the bulb is generally at the level of the 1st to 2d lumbar vertebrae. Variations in its size seem to depend on variations in the tonus of its walls and it may vary in the same individual at different times with changes of tonus. An unusually small bulb is often seen in duodenal ulcer due to spasm. Generally the position of the bulb is on the right side of the midline and it is found on the left only in cases of marked Rieder stomach. The width of the upper abdomen has a marked influence on the position of the bulb. There may also be elongation and angulation of the extrabulbar part of the duodenum with a real inversion of direction and there may be a adhesions and angulation between the first and second portions of the duodenum. There is another not unusual anomaly of the first portion consisting of a "festoon loop" which hangs between the apex of the ampulla and the upper flexure of the duodenum. This is a congenital anomaly caused by ptosis of the ligaments secondary to ptosis of the organs to which they are attached. The normal course of the second portion of the duodenum lies laterally from the bulb but in some cases it lies to the median side of the bulb, constituting a true anomaly. From this simple anomaly there are all gradations to the most complex ones with elongation and inversion of the second portion. These anomalies are, beyond doubt, congenital. There is sometimes an angulation of the second portion which Balli calls scoliosis of the second portion. It is sometimes hard to tell whether this is congenital or caused by traction from adhesions But when the angulation is combined with elongation it is generally congenital and a prelude to partial dolichoduodenum. In some cases, particularly those with a V-shaped duodenum, there is sometimes an arrest of the contrast medium at the lower flexure; these are the cases in which an anomalous crossing of the mesenteric vessels causes compression of the duodenum with a characteristic roentgen symptomatology, which is illustrated.

In partial free duodenum only the third portion of the duodenum is mobile while in total free duodenum the whole of the duodenum is mobile. This is an anomaly in development and rotation of the organ. It rarely causes subjective disturbances of any importance.—*Audrey G. Morgan.*

Anzilotti, Alberto. L'esame radiologico dell'apparato digerente negli intossicati cronici da piombo. (Roentgen examination of the digestive tract in chronic lead poisoning.) *Radiol. med.*, Mar., 1931, *18*, 356–381.

The author made a roentgen study of the digestive tract in a number of cases of chronic lead poisoning. Roentgen examination showed intermittent gastric hyperperistalsis, persistent hypertonus of the antrum, spasm of the duodenum, more rapid passage than normal through the small intestine, intense spasm of the colon at the site of the attacks of pain and considerable retardation in the evacuation of feces; there was pain on pressure in the aorticoiliac region. He then discusses the significance and value of each of these signs, all of which in combination give a roentgen picture of considerable value. He then discusses differential diagnosis from other chronic intoxications that affect the digestive tract and gives brief clinical histories of 14 cases illustrated with roentgenograms.—*Audrey G. Morgan.*

Harbin, R. M. Meckel's diverticulum. *Surg., Gynec. & Obst.*, Dec., 1930, *51*, 863–868.

Post-mortem records show in general an incidence of diverticula of about 2 per cent. Harbin reports 10 per cent of their cases of intestinal obstruction as due to Meckel's diverticulum. Wellington reports 6 per cent of the cases of intestinal obstruction as due to Meckel's diverticulum. A history of a discharge from the umbilicus in infancy can usually be obtained from cases in which diverticula are later found,

according to Balfour. Harbin found 19 cases in his surgical cases in which a preoperative diagnosis had been made in only one case. This article deals essentially with the surgical aspect of Meckel's diverticula.

There is a rather complete bibliography attached.— *J. H. Vastine.*

BAGNARESI, GIACOMO. Sulle ectopie del cieco e del colon ascendente. (Ectopy of the cecum and the ascending colon.) *Arch. di radiol.*, Jan–Feb., 1931, *7*, 1–19.

Two cases of subhepatic ectopy of the cecum which were diagnosed roentgenologically are briefly reported and in connection with this the possible causes are discussed. It is important that a roentgen examination of the entire gastrointestinal tract be made with films in the oblique and lateral projection. Clinically in both instances there was rather marked pain which was of a periodic character, coinciding generally with the passage of the food through that portion of the intestinal tract. It is the author's opinion that this periodic pain when associated with persistence of morphologic alterations, as demonstrated roentgenologically, may direct the attention towards the correct diagnosis.—*T. Leucutia.*

LARIMORE, JOSEPH W. Roentgenology of the appendix. *Surg., Gynec. & Obst.*, Dec., 1930, *51*, 810–822.

Roentgenology seems to establish concurrent alimentary disease when it is present; therefore, when appendicial involvement is suspected a full gastrointestinal examination including cholecystography should be made. Ulcer and cholecystitis are often associated with and sequelae to chronic appendicitis. Solieri calls this association of the three conditions the "pathological harmony of the right abdomen."

Visualization or non-visualization of the appendix is not significant in indicating the presence or absence of appendicial pathology. Pathological changes in the appendix are revealed by changes observed in the barium-filled lumen. This is a dependable finding. *Stricture, filiform reduction of the lumen, stiffening of the wall* and *bulbous distention* are pathognomonic of anatomical changes but are not conclusive of clinical appendicitis. They may be residual only. Abnormal position may be congenital, in which case it is usually retrocecal. Acquired abnormal fixation is due to inflammatory penetration of the wall with resulting adhesions. *Retention* of barium in the appendix after emptying of the cecum and ascending colon is significant. *Concretions* are significant in the diagnosis of disease, as shown by Archibald, and are represented by a filling defect in the barium-filled appendix. Roentgenology has shown the inconstancy of McBurney's point since there is normally such a wide range of position of the appendix. Tenderness is not present upon palpation of the normal appendix. Tenderness due to appendicial involvement to be characteristic must be localized to the original of the appendix from the cecum. Palpable tenderness of the appendix is often referred to the umbilicus or to the epigastrium. Incompetence of the ileocecal valve in a dilated cecum is not significant. Incompetence of the valve when the cecum shows good tonus is a supplementary sign of appendicial disease. Signs of peritoneal irritation such as atypical, patchy, irregular, discrete loops of small intestine while not pathognomonic of appendicitis furnish valuable diagnostic evidence. Appendicial abscess which is localized and subacute may be diagnosed by evidence of peritoneal irritation, displacement of the ileum and cecum.

The information obtained relative to the appendix must be correlated with the clinical findings.

This article is profusely illustrated.—*J. H. Vastine.*

PEROTTI, DESIDERIO. Calcinosi peritoneale. (Peritoneal calcinosis.) *Radiol. med.*, Mar., 1931, *18*, 381–386.

The author describes a case of peritoneal calcinosis in a girl aged seventeen, which had affected the whole peritoneum; in the roentgenograms it was dotted with innumerable small calcareous spots. The condition was discovered by chance in this patient with lumbar spondylitis who had previously had specific peritonitis. The author thinks the calcinosis resulted from tuberculous nodules scattered in the peritoneum and says that such a roentgen finding would probably always be by chance, for this disease, even when it is diffuse, may develop without any special clinical signs.—*Audrey G. Morgan*

BILGER, F., and FONTAINE, R. A propos de quelque observations de lithiase biliaire et d'affection rénale intriquées. (Some observations on biliary lithiasis in combination with puzzling renal affections.) *Rev. de chir.*, Jan., 1931, *50*, 34–47.

The authors report 5 cases in which an affection of the gall-bladder coexisted with one of the kidney. In 3 cases the right kidney was affected and in 2 cases the left. In all of the 5 cases gallstones were found, verified roentgenographically, and in 4, verified by operation.

The renal conditions were always unilateral. In 4 cases a simple pyonephrosis was present, but in 2 of these ptosis of the kidney was also noted. In the fifth case a left renal calculus was discovered in a hydronephrotic or polycystic kidney. In all of the cases the causative agent was the colon bacillus.

The authors discuss the various theories of pathogenesis and etiology of these conditions and their apparent relation one to the other. Some have claimed the renal pathologic change as the primary cause of the biliary condition and others have claimed the opposite. They do not attempt to decide the question.

In regard to the symptoms, the abdominal complaints may be passed over by the surgeon as reflex phenomena from the renal condition. If the biliary symptoms manifest themselves before those of the urinary tract, the urologist will often first see the patient. They believe that the biliary symptoms often are entirely overlooked.

In regard to diagnosis, they regard the projection of the calculus shadow in the lateral view of extreme value. Cholecystograms should always be employed but they have had one case in their experience in which a shadow of an apparent stone lay just beyond that of the gall-bladder and a diagnosis was made from the cholecystograms of a stone in the common duct. The lateral view, however, showed the shadow of the stone on a level with the vertebral bodies, thus proving it was of renal origin.—*R. S. Bromer.*

Garcin, Joseph, and Sarles, Roger. Résultats comparés de l'epreuve de Meltzer-Lyon et de la cholecystographie. (Comparative results of the Meltzer-Lyon test and cholecystography.) *Bull. et mém. Soc. de radiol. méd. de France*, April, 1931, *19*, 190–192.

In a total of 754 cases examined by cholecystography, a non-filling of the gall-bladder was found in 14 per cent. During the same period, in 98 cases examined by the Meltzer-Lyon functional test (with duodenal tube) a non-function of the gall-bladder was found in 12 per cent. Of 78 well-selected cases which were examined comparatively by both methods a few days apart, cholecystography led to positive results in 64 and the Meltzer-Lyon test in 68. Thus, the conclusion is reached that there is a strict parallelism between cholecystography and the Meltzer-Lyon functional test in the study of gall-bladder conditons. Their association of the two methods leads to very accurate information.—*T. Leucutia.*

Renander, Axel. Einige röntgenologisch beobachtete Fälle von Magentuberkulose. (Some cases of tuberculosis of the stomach studied roentgenologically.) *Acta radiol.*, Dec. 31, 1930, *11*, 636–648.

In spite of the great frequency of tuberculosis of the lungs and intestine, tuberculosis of the stomach is extremely rare. Local tuberculosis of the stomach may be of either the ulcerous or the hypertrophic type and Poncet describes a third acute inflammatory form. In the majority of cases the disease is localized in the canalis ventriculi. Complications such as hemorrhage and perforation are rare. The symptomatology is not characteristic; the prognosis is serious.

The author has seen 3 cases of tuberculosis of the stomach that were clinically primary but in 2 of them roentgen examination showed old healed foci in the lungs. In one case the process was localized in the body of the stomach, in the other 2 in the canalis ventriculi. Two of the cases were verified by microscopic examination; in the third a mesenteric gland was found. The symptoms were not characteristic. In 2 of the cases resection was performed; in the third, gastroenterostomy. One of the patients has been under observation for two and a half years, the others for some months and all are free of symptoms. Roentgenograms of all the cases are reproduced. That of Case 1 showed a peculiar appearance which suggested infiltration from some unusual cause.—*Audrey G. Morgan.*

Bastian, G. Ein Fall von multipler Divertikelbildung des Duodenums. (A case of multiple diverticula of the duodenum.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Nov., 1930, *42*, 610–612.

This is a case report of multiple diverticula of the duodenum which occurred in a man sixty-seven years of age. Two diverticula were found at the level of the papilla of Vater (one on the anterior and one on the posterior wall), one at the median border of the ascending portion and two in the inferior portion of the duodenum.—*T. Leucutia.*

BERGSMA, STUART. Gastric and duodenal ulcer in the black people of Abyssinia. *Arch. Int. Med.*, Jan., 1931, *47*, 144–148.

The author reviews the literature on gastric and duodenal ulcer occurring in negroes, and comes to the conclusion that it is a rare condition in this country. His experience in Abyssinia, however, was quite different. Gastric and duodenal ulcers are not rare in the black race, and he therefore comes to the conclusion that there is nothing in the black race per se that makes gastric ulcer uncommon in negroes of the United States.

He believes the first factor in the production of gastric ulcer among the Abyssinians is an unusually high red pepper content of the diet. He records the fact that appendicitis is rarely seen among the negroes of Abyssinia.—*E. P. Pendergrass.*

DRENNEN, EARLE. Ileocecal cysts. *Arch. Surg.*, Jan., 1931, *22*, 106–120.

Cysts of the ileocecal region constitute a definite pathological surgical entity. That there are enterogenous developmental cysts there can be no doubt. While the nature of these cysts is not well understood the cause of their origin remains obscure. In many of the lower animals the arrangement of the cecal pouches is suggested Ileocecal cysts are rare. A search of the literature yields but 20 cases, and the author of this article adds three. He includes in the article a detailed summary of the 20 cases reported in the literature. From his study it seems to be evident that many cases have been overlooked, and with a growing appreciation of the condition one may expect a marked increase in the number of cases.

Cysts and diverticula of the intestine apparently escaped the notice of the older pathologists. In the small intestines they are easily observed because they are found between the leaves of the mesentery where the vessels pierce the walls of the intestine, leaving a point of lessened resistance.

In the large intestine, however, the muscle hernias or diverticula escape into the fatty appendices epiploicae, also a spot of lessened resistance. Owing to the fact that these diverticula are covered with fat it is easy to understand their being overlooked. Roentgen examinations often reveal their presence when they are not suspected.

Cysts and diverticula of the intestines are in reality different phases of the same process, and the author describes the embryological theories in regard to their development.

The diagnosis of ileocecal cysts, and cysts of the cecum, is by no means easy, and even at the time of operation they may be overlooked. A movable tumor in the region of the cecum is suggestive. A large percentage of the cases have shown symptoms of acute or recurring obstruction. Both patient and surgeon will fare well if resection of the intestine is done. In no case has the attempt to enucleate the cyst been successful. Malignancy has not been noted in connection with these cysts.—*E. P. Pendergrass.*

CARLSON, H. A., DVORAK, H. J., LYNCH, F. W., BORMAN, C., and WANGENSTEEN, O. H. Value of x-ray evidence of bowel obstruction in various states of intestinal stasis. *Proc. Soc. Exper. Biol. & Med.*, Dec., 1930, *28*, 343–344.

Roentgenograms of dogs with obstructed loops usually revealed some evidence of gas in the obstructed loop at the end of eight or ten hours, but the appearance of definite gaseous distention was an inconstant finding occurring as early as eight hours but in some cases not being definite after more than 100 hours. Fluid levels were demonstrable in some of the loops.

After mesenteric vein ligation roentgenograms were negative in 2 dogs which died early and in the normal which recovered from the operation. Gaseous distention was variable, being seen best at twenty-three hours, seventy-two hours and five days. Gaseous shadows were observed early (1 to 11.5 hours) in 4 cases of peritonitis, but could not be satisfactorily demonstrated in 2 dogs dying at thirteen and twenty hours.

From the experiments one may conclude that although roentgenographic evidence of gaseous distention is an early and valuable sign of simple intestinal obstruction, it is distinctly of less value in strangulation obstruction or in stasis due to mesenteric vein occlusion. Gas shadows are also observed early as a rule in peritonitis. —*B. Cohen.*

WALZEL, P. Zur Möglichkeit der röntgenologischen Beurteilung von Anomalien und Variationen der Gallenblase. (The possibility of roentgen evaluation of anomalies and variations of the gall-bladder.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Nov., 1930, *42*, 635–639.

The roentgen examination may be of value in the diagnosis of certain anomalies and variations of the gall-bladder. The anomalies include: situs inversus, aplasia or hypoplasia, the persistence of certain embryonal conditions such as ductus hepatico-cysticus, accessory gall ducts, etc., double gall-bladder and double ductus cysticus, septum gall-bladder, vesica fellea occulta, Luschka's ducts, and transverse fixation of the gall-bladder.

The individual variations may consist in a modification of the peritonealization of the gall-bladder, in a total imbedding in the liver parenchyma, in variation of the form (kinking, hour-glass form, etc.), in variation of the relation to the neighboring organs (persisting ligamentum cysticoduodenale, cystico-colicum, hepatocystocolicum, etc.), and finally, in "regeneration of the gall-bladder" following operation, which in fact is a passive dilatation of the remaining stump of the ductus cysticus.—*T. Leucutia.*

Delario, A. J. Paths of absorption and excretion of sodium tetraiodophenolphthalein. *J. Lab. & Clin. Med.*, Jan., 1931, *16*, 329–340.

This is an excellent article, and everyone employing this test should read it.

During the course of an intravenous Graham test a shadow appears in the large intestine. This shadow may be either uniform in density, or of a homogeneous nature. When the dye is given orally two different types of shadows may appear in the large intestine: one, a uniform, homogeneous shadow, the other, a shadow of increased granular density. The latter shadow represents unabsorbed particles or clumps of dye which did not dissolve. A question arises as to what is the source of this uniform, homogeneous shadow. Is it dye which has come down the common duct and passed to the large intestine? Is it dye which has been excreted by the large intestine? Is it dye which is being absorbed by the large intestine? When the dye is given orally, can any have passed through the small intestine in this uniform state, without being absorbed? What is the clinical significance of this dye in the large intestine?

Results of the oral administration of dye have been shown by Robins and Goldberg to be unsatisfactory. In a report of 1000 cases, 502 cases showed a good gall-bladder outline, 343 cases showed a poor gall-bladder outline, and 169 cases showed no gall-bladder outline. In 50.49 per cent of the cases, therefore, the gall-bladder showed abnormal results. The question arises as to whether the gall-bladder is pathological, or the dye not absorbed.

From the experimental data on absorption and excretion of the dye included in this paper, the author found that when the dye is given intravenously from 50 to 75 per cent of the shadow in the large intestine is due to dye being eliminated from the common duct by the way of the small intestine. He also found that 25 to 50 per cent of the shadow is due to dye being excreted by the large intestine. No matter how the dye is given, the unabsorbed dye will be in a clump or in a granular form, and can be readily distinguished from that excreted by the liver or large intestine.

When given in a uniform solution, as in grape juice, the acid of the juice, as well as the hydrochloric acid of the stomach, causes precipitation. Most of this precipitated dye is rendered soluble and absorbable by the alkaline juices of the small intestines, but apparently some of it is not. The bile and dye excreted by the liver during fasting enter the gall-bladder because the sphincter of Oddi is, for the most part, closed. Some bile and dye are allowed to pass through, however. During the first twelve hours of fasting after an intravenous Graham test the greatest part of the bile flows to the gall-bladder. It requires food to furnish the necessary stimulation to open the sphincter of Oddi. Thus, the shadow at this time in the large intestine represents the dye excreted by the large intestine, and the small amount that has passed by the cystic duct and out into the small intestine.

The author believes that the homogeneous shadow seen in the large intestine after the administration of the dye intravenously and by mouth can be of assistance in the diagnosis of gall-bladder disease in the following way: If the shadow of the gall-bladder and that of the large intestine are of normal density, the gall-bladder and cystic duct, the common duct, and the sphincter of Oddi are normally functioning; if there is a shadow in the large intestine and none in the gall-bladder, there is some disturbance in the function of the gall-bladder, or obstruction to the cystic or common duct (or incompetence of the sphincter of Oddi, with normal gall-bladder and cystic duct); if the gall-bladder shadow is weak or faint, and that of the large intestine is dense and large, the author suggests either poor absorption by the gall-

bladder (or increased absorption), or a constriction of the cystic or common duct, or a pathological dilatation of the hepatic and common bile ducts, and incompetent spincter.

The author carried out a number of experiments on dogs, and found out that the rate of disappearance of the dye from the blood stream was two to four hours. The rate of disappearance of the dye from the liver is one to two hours, when it is given intravenously. The maximal concentration of the iodine in the bile occurs about five hours after the administration of the dye. The urine eliminates approximately 5 per cent of the dye except in cases of common duct obstruction. The large intestine was found to eliminate the dye directly, and is supposed to eliminate approximately 25 per cent of the dye.

The author found that the dye eliminated by the liver was rendered insoluble, probably not changed or conjugated. He also found that a small amount of the dye that was eliminated by the common duct was precipitated by the pancreatic juice and passed through the intestine unabsorbed. The action of the fat on the dye causes great precipitation, and Delario suggests that this may be one of the ways in which fat causes a diminution in the size of the gall-bladder shadow. The dye is eliminated by the kidneys in both the inorganic and organic state. —*E. P. Pendergrass.*

BECKER, RUDOLF, and OPPENHEIMER, ALBERT. Der physiologische Ablauf der Dickdarmbewegungen. (The physiology of the movements of the colon.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Dec., 1930, *42*, 730–739.

The barium meal is propelled by a rhythmic peristalsis from the terminal ileum into the cecum. After passing the cecocolic sphincter it is further advanced by a continuous mixing movement to the splenic flexure. During this time the haustra of the ascending and transverse colon appear polymorphous indicating active peristalsis. After the head of the barium column has reached the splenic flexure a rest period sets in, lasting for twenty-four hours, during which period the haustra appear isomorphous, indicating non-activity. The descending colon shows practically no or only sluggish peristalsis, the evacuation occurring chiefly by gravitation (vis a tergo). After the sigmoid is filled the defecation mechanism sets in.

The article is illustrated with several roentgenograms showing the various appearances of haustrations.—*T. Leucutia.*

GYNECOLOGY AND OBSTETRICS

MATTHEWS, HARVEY B. The roentgen ray as an adjunct in obstetric diagnosis. *Am. J. Obst. & Gynec.*, Nov., 1930, *20*, 612–632.

The fact that roentgenography is not employed in the practice of obstetrics and gynecology to the greatest extent of its usefulness is discussed by the author. The author quotes convincing literature to dispel any fear of damage to the fetus due to diagnostic roentgenology in competent hands. With regard to dangers to the fetus, the author, an obstetrician, says, "We feel sure that no pregnancy, regardless of its stage of development, is damaged by diagnostic roentgenology properly carried out." The conditions in which the roentgenologist can furnish valuable information to the obstetrician are enumerated as follows:

Those relating to the maternal pelvis: (1) deformities; (2) pelvimetry; (3) bony or calcified pelvic tumors; (4) separation of symphysis, and (5) amount of healing after pubiotomy.

Extrauterine pregnancy.

Those relating to intrauterine pregnancy: (1) positive diagnosis of pregnancy as early as fourteenth week; (2) multiple pregnancy; (3) presentation and position of fetus; (4) cephalometry; (5) death of fetus; (6) monsters, anencephalus, hydrocephalus, etc.; (7) spina bifida and other skeletal defects; (8) syphilis of fetal bones; (9) hydatidiform mole (by exclusion); (10) intrauterine fractures; (11) osteogenesis imperfecta; (12) illegitimate pregnancies where no examination can be made; (13) routine examination should be made before cesarean section to determine if the child is normally formed.

Differentiation of a pelvic tumor from pregnancy: (1) myomata; (2) myomata and pregnancy; (3) ovarian cysts, dermoids, etc.

Miscellaneous conditions: (1) spontaneous version; (2) pseudocyesis; (3) mechanism of labor; (4) mode and method of seperation of placenta (Warnekros); (7) proof of extrauterine life (Vogt).—*J. H. Vastine.*

GENITO-URINARY SYSTEM

BEER, EDWIN. Uroselectan intravenous urography. *Ann. Surg.*, Oct., 1930, *92*, 761–765.

A short article on intravenous urography in

which a brief reference is made to the history of this method of examining the urinary tract along with the advantages and disadvantages as compared to retrograde urography. The necessity of experience in interpretation of roentgenograms obtained by intravenous urography is emphasized.

The article is illustrated with six roentgenograms depicting various urological conditions. —*Karl Kornblum.*

Kidd, Frank. Intravenous pyelography. *Lancet*, July 19, 1930, *2*, 128–132.

Uroselectan, provided by Binz and used by von Lichtenberg and Swick, contains 42 per cent of iodine. In the passage of the substance through the body none of the iodine is given off in an ionized form. Hence no toxic effects arise.

Clinically 40 gm. of uroselectan are dissolved in 100 c.c. of distilled water and injected intravenously. The drug is never given by mouth. When both kidneys function normally there is excretion in a few minutes of urine sufficiently radiopaque to cast a shadow on the roentgenogram. Films are made routinely at 15, 45 and 75 minutes after injection. When kidney function is deficient excretion may be delayed. Micturition before each examination is required to avoid obscuring the lower ureters by a full bladder.

In 17 cases, a satisfactory result was obtained in 11, a doubtful one in 3, and one of no value in 3. Cases of renal tumor and inflammation yield poor pictures, while cases of obstruction yield good ones.

Intravenous urography should be reserved at present for cases where cystoscopy and catheterization of the ureter are difficult, dangerous or impossible.

Interpretation presupposes the realization that inflamed kidneys may cease to function either permanently or temporarily and hence cast no shadow. Renal tumors similarly may interfere with function. Normal systolic contractions may obliterate portions of the calyces and ureters. Interpretation is difficult.

The functional value of each kidney can be estimated by observing the time and density of the appearance and disappearance of the roentgen shadows.—*G. R. Miller.*

Heritage, Kenneth. Intravenous pyelography. *Lancet*, July 19, 1930, *2*, 132.

In all cases in which a satisfactory shadow appeared in the roentgenogram within half an hour after the injection of uroselectan there was found a considerable amount of normal kidney tissue. Although the ability eventually to excrete enough of the dye to cast a pelvic shadow was retained in cases of quite severe renal damage, yet the failure to excrete enough to give such a shadow was significant of an organ so completely disorganized as to be obviously functionless. Rapid emptying of calyces and ureters in cases of normal function denoted by satisfactory bladder shadows can be overcome by slight ureteral compression best applied by pads.—*G. R. Miller.*

Asti, Mario Luigi. Considerazioni sul valore della pielografia endovenosa con l'Uroselektan nell'indagine radiologica del rene e delle sue cavita. (The value of intravenous pyelography with uroselectan in the roentgen examination of the kidney and its pelvis.) *Radiol. med.*, Jan., 1931, *18*, 42–115.

The author first gives a general discussion of the new method of pyelography with uroselectan and describes its technique. He also considers the degree of tolerance shown by different patients, the indications and advantages of the method and the results which it has given. He says that considerable numbers of cases have already been reported in the literature in which the interpretation of the pictures was doubtful because of lack of opacity or because the outlines were indistinct, while in some cases the picture did not show what really existed. He tries therefore to determine the cases in which the method is reliable and those in which it is not. Good pyelograms have been obtained in cases of obstruction to the flow of urine, congenital malformation, topographical changes, hypertrophy of the prostate, urethritis, cystitis and pyelitis in pregnant women and little children. But the pictures have not been reliable in various kidney diseases, including tuberculosis, hydronephrosis, polycystic kidney, tumor and even in kidneys that were later found to be normal. In determining the value of a new method it is more important to consider the cases in which the results are negative or insufficient than those in which they are positive.

He then describes 18 cases examined at the Radiological Institute of the University of Milan. Most of them were gynecological cases from the Cancer Institute and were in advanced stages of epithelioma of the uterus. Some of the cases were controlled by ascend-

ing pyelography and some of them by autopsy. The author found the method absolutely harmless but he concludes from his experience that intravenous pyelography alone rarely gives reliable information in regard to the pathological condition. It should always be confirmed by retrograde pyelography. In some cases the intravenous pyelogram has seemed to show pathological conditions while the kidney pelves were found normal on retrograde pyelography. He does not believe that intravenous pyelography with uroselectan can replace instrumental pyelography but it may be a valuable supplement to it and should be used in all cases in which ascending pyelography is contraindicated or impossible.—*Audrey G. Morgan.*

LAROCHE, ALBERT. Intravenous pyelography. *Canad. M. Ass. J.*, Sept., 1930, *23*, 414–416.

The author briefly reviews the history of the development of pyelography by the intravenous method. The advantages which pyelography by the intravenous method enjoys over pyelography by the retrograde method, are the wide application of this method; the practical absence of contraindications to the method; the information relative to the functional activity of the kidneys, and the excellent cystograms which can be coincidently obtained.—*J. H. Vastine.*

SKELETAL SYSTEM

POMERANZ, MAURICE M. Roentgen diagnosis of bone tumors. *J. Bone & Joint Surg.*, Oct., 1930, *12*, 795–818.

In this article the author reviews the subject of bone tumors, primarily from the viewpoint of the roentgenologist. The various and diverse changes any bone tumor may produce are many and experience has taught the careful roentgenologist to be extremely cautious in his interpretations.

In diagnosing bone tumors it is necessary to remember the changes in osseous structures, the result of an inflammation, and as most of the changes seen in osteomyelitis are encountered in bone tumors the differential diagnosis may be extremely difficult.

The author summarizes the differential diagnosis of the general characteristics of bone lesions as follows:

Osteomyelitis

Single or multiple
Sharp or irregular border
Involvement of medulla, cortex, periosteum or combined.
No bone expansion
Destruction solely within bone
Osteoblastic and osteoclastic changes within lesion
No soft tissue involvement
Periosteal thickening
Parallel bone deposit
Sequestration
Slow development

Benign tumors

Localized as a rule
Sharp, limiting border
Limitation to either medulla, cortex or periosteum
Bone expansion great
Tumor within bone, except cortical group
Either osteoblastic or osteoclastic
No soft tissue involvement
No periosteal stripping
Parallel bone deposit in pseudo-neoplastic group
Slow development

Malignant tumors

Single or multiple
Irregular invasion
Involvement of cortex, medulla and periosteum simultaneously
Bone expansion slight
Tumor in and about bone
Osteoblastic or osteoclastic changes within same tumor.
Soft tissue involvement
Periosteal stripping
Perpendicular bone deposit
Rapid development

The author presents the following classification of bone tumors as a help towards a working diagnosis

Benign	Cortical osteoblastic	(a) osteoma (b) osteochondroma (c) exostosis (d) pseudoneoplastic
	Medullary osteoclastic	(a) enchondroma (b) giant cell tumor (c) cysts (d) osteitis fibrosa cystica
Malignant	Primary	(a) osteogenic (b) Ewing's tumor (c) multiple myeloma (d) unusual types
	Metastatic Osteoclastic and Osteoblastic	(a) prostate (b) breast (c) thyroid (d) kidney (e) lung

A short roentgen description is given pointing out the characteristic appearances of the individual tumors.—*F. K. Alexander.*

Morton, Charles B. Osteogenic sarcoma of the humerus. *Arch. Surg.*, Sept., 1930, *21*, 444–457.

The author reports a case of telangiectatic osteogenic sarcoma of the humerus occurring in a mulatto boy aged seventeen. The tumor attained immense size in the short period of four months, from the onset of the first symptom to the death of the patient. The case is discussed briefly from the standpoint of the pathology, diagnosis and treatment. Practically the only treatment given was the use of Coley's toxins, which did not seem to be of any value in this case. Amputation was not done. The article is accompanied by illustrations of the patient at various stages in the growth of the tumor and by excellent photomicrographs of sections of the tumor.

A brief résumé is made of the recent literature on osteogenic sarcoma with special reference to material from the Registry of Bone Sarcoma.—*Karl Kornblum.*

Bergstrand, Hilding. Über eine eigenartige, wahrscheinlich bisher nicht beschriebene osteoblastische Krankheit in den langen Knochen der Hand und des Fusses. (A peculiar osteoblastic disease in the long bones of the hand and foot that has probably not been described before.) *Acta radiol.*, Dec. 31, 1930, *11*, 596–613.

The author describes 2 cases of a disease which he says has not been described before. The patients were sixteen and eighteen years of age. In the first patient, a girl of sixteen, there was enlargement of the 2d metatarsal of the right foot and in the second patient, a young man of eighteen, enlargement of the basal phalanx of the left middle finger. In both cases there was swelling, pain and impairment of function. Roentgen examination showed enlargement of the bone and in one of the cases there was decreased opacity of the shadow at the enlarged end of the diaphysis. The cases were diagnosed as osteogenic sarcoma and operation performed. In one case resection was performed, in the other exarticulation. Histological examination showed a new growth that was neither tumor nor inflammation. It evidently originated from a focus at the area of decreased density mentioned above. It was made up of a central amorphous collagenous substance surrounded by a very vascular area of spongy bone. From this zone vessels and osteoblasts penetrated the central mass. The author thinks the process was embryonic in origin. This conclusion is based partly on the youth of the patients.—*Audrey G. Morgan.*

Bermond, Marco. A proposito di quattro casi di sesta vertebra lombare soprannumeraria. (Four cases of supernumerary sixth lumbar vertebra.) *Radiol. med.*, Jan., 1931, *18*, 18–36.

The author gives the case histories of his 4 cases of supernumerary sixth lumbar vertebra and illustrates them with roentgenograms. He found these in the course of roentgen examination of 158 spinal columns, constituting 2.5 per cent of the total number of cases. This is much lower than the percentage usually given but most authors do not make a distinction between purely supernumerary vertebrae and morphological anomalies of the region. These supernumerary vertebrae can only be demonstrated by accurate counting of all the vertebrae. There are cases of pure numerical variation without any malformation of the supernumerary metamere but these are very rare—only 0.65 per cent. Most of the cases are ones of mixed variation, both numerical and morphological. This kind of anomaly is most frequently seen in the lumbosacral tract and in the majority of cases the supernumerary vertebra is a sixth lumbar. None of the pure numerical variations cause any changes in the statics of the spinal column and some of the mixed variety do not, but in some of the mixed variety there is asymmetrical development with severe deformity. The cause of these anomalies is a deviation of embryonic segmentation probably accompanied by similar anomalies in the other embryonic layers; these anomalies could not be attributed either to hereditary factors nor to disturbances of internal secretion in the author's cases. Nor can they be considered atavistic. The pure numerical anomalies do not cause any subjective symptoms; the mixed forms may cause lumbosacral pain or sciatica such as occurs in sacralization of the fifth lumbar vertebra.—*Audrey G. Morgan.*

Macchioro, Gino. Un caso di aplasia parziale del costato destro con ipotrofia e sindattilia della mano corrispondente. (A case of partial aplasia of the right ribs and syndactyly of the corresponding hand.) *Radiol. med.* Jan., 1931, *18*, 37–42.

A child two years of age was brought to the

hospital for an ordinary bronchitis. The child was mentally normal for its age. The right hand was much less well developed than the left and there was syndactyly between the 2d and 3d and the 3d and 4th fingers. There was a marked depression, roughly triangular in form, in the right side of the child's chest wall. A roentgenogram showed that the 2d, 3d, 4th and 5th ribs were lacking from the posterior axillary line to the midclavicular line. There was a slight scoliosis of the spinal column. No changes in the skull or teeth.

The author thinks this anomaly was due to pressure of the child's fist on the wall of the thorax during the early months of intrauterine life. This would explain the anomalies of the hand as well as those of the ribs.—*Audrey G. Morgan.*

LOVISATTI, NICOLA. Il comportamento del callo di fratture nelle ossa irradiate. (The callus in fracture of irradiated bones.) *Radiol. med.*, Jan., 1931, *18*, 1–8.

The author irradiated the right front paws of 9 rabbits with a dose of 30 H. In 3 of them he fractured the radius of both front legs thirty days later and in the other 6 sixty days later. The bones on the left side were fractured for controls. He found that the callus formed on the non-irradiated side in twenty to twenty-five days while it required ten to forty days longer to form on the irradiated side in both groups of animals. In the irradiated animals the callus was not only retarded in development but it was smaller than usual. There was no special difference in the animals irradiated thirty days before the fractures and those irradiated sixty days before so far as the process of repair was concerned. The reaction seemed to be less intense in adult animals than in young ones.—*Audrey G. Morgan.*

BLOOD AND LYMPH SYSTEM

HAMBURGER, LOUIS P. Angina agranulocytica and its treatment. *Johns Hopkins Hosp. Bull.*, May, 1931, *48*, 339–348.

This disorder which usually occurs in older women, is manifested by local necrotic lesions and swelling in the throat, and a generalized leucopenia with markedly diminished granular elements in the blood. The blood changes probably precede the sore throat and more routine examinations of the blood in private practice would no doubt lead to earlier and more frequent diagnosis. The evidence collected to date suggests that the various organisms reported in the blood stream are secondary invaders, the primary disorder being in the depressed function of the granulocytic system.

Fifteen cases are used in this study which fall into four groups: the fulminating type with early death, the prolonged illness with death or recovery in a few weeks, the recurrent type with a history of several attacks, and a subchronic type, with an illness of several months. Reference is made to a reported case of chronic agranulocytic angina which persisted from infancy in a man twenty years of age.

Many forms of treatment are suggested but the best results have been obtained by repeated transfusions of citrated blood, vigorous local treatment and cautious irradiation of the skeleton by an expert roentgen therapist. Though there is a diversity of opinion regarding the benefits of irradiation this method should be used.—*E. W. Hall.*

WATERS, CHARLES A., and FIROR, WHITMER B. Roentgenotherapy of angina agranulocytica. *Johns Hopkins Hosp. Bull.*, May, 1931, *48*, 349–351.

Skepticism has been expressed regarding roentgen therapy in agranulocytic angina and concerning irradiation of bone marrow. Friedemann, Moldowski and others have reported a number of cases which recovered following the use of one-twentieth of an erythema, or so-called stimulating dose, copper filtration being apparently more efficacious than aluminum. The authors report 5 cases, 4 of which apparently recovered. The fifth died, having been almost in extremis when treatment was given. The lower extremities, pelvis, upper humerus and shoulder girdles were irradiated in the course of three or four treatments. Voltage values of 200,000 with aluminum and copper filtration both separately and combined, with effective wave length ranging from 0.197 Å to 0.161 Å were used. Dosage measurements, which must be accurate where such a small dose is to be used, was made by a dosimeter reading in International r.

The actual evaluation of the effect of irradiation is difficult due to the use of other measures which may have influenced the course of the disease. There is no evidence that a cell per se is affected by the roentgen ray other than in a destructive manner. However, definite in-

crease in reticulocytes and other blood cells has been noted following small roentgen treatments.

The results obtained justify a trial of irradiation of bone marrow in this disease wherever possible.—*E. W. Hall.*

Uspensky, A. Die Bedeutung der Röntgenstrahlen für die Diagnose der Lymphogranulomatose. (The importance of roentgen rays in the diagnosis of lymphogranulomatosis.) *Fortschr. a. de. Geb. d. Röntgenstrahlen*, Nov., 1930, *42*, 617–634.

Eighteen cases of lymphogranulomatosis are briefly described and illustrated with roentgenograms and photographs. The roentgen examination is of value in detecting a primary lesion of the mediastinum before there is any other manifestation of the disease, in observing secondary manifestations within the chest if the lesion is already generalized and in revealing the presence of occlusion atelectasis or association of tuberculosis. In the gastrointestinal tract the roentgen examination leads to a detection of ulcers or tumor masses similar to those observed in malignancy. Pneumoperitoneum, on the other hand, permits the recognition of involvement of the retroperitoneal lymph nodes. In case of involvement of bones a roentgen examination may reveal an osteoporosis or an eburnation.—*T. Leucutia.*

Bonta, Maurice B. Splenectomy in Gaucher's disease. *Arch. Surg.*, Nov., 1930, *21*, 851–859.

The author records 4 cases in which splenectomy was performed. The histories are given in detail. All of the patients were women. The ages ranged from twenty-six to thirty-six years. There was no history of a familial tendency. Two patients were Hebrews. Gaucher's disease may not affect the health of the individual. Splenomegaly is the chief complaint. One patient died two years after splenectomy. The others are living from seven months to ten years. Of 530 cases in which splenectomy was performed only 4 showed evidence of Gaucher's disease. The blood picture was not characteristic. The diagnosis may be made by removal of a lymph node, splenic puncture, bone marrow trephine, or roentgen appearance of involved bones. Splenectomy is not a curative but a palliative procedure.—*E. P. Pendergrass.*

GENERAL

Roffo, A. H. Cáncer post traumático. (Post-traumatic cancer.) *Bol. Inst. de med. exper. (etc.)*, Buenos Aires, 1930, *7*, 204–277.

In endeavoring to interpret post-traumatic tumor formations one must consider two factors: (1) the so-called biologic "terrain" and (2) the determining cause. The first depends on the physicochemical state of the tissues; the second may consist of a single trauma or repeated chemical, physical and mechanical irritations.

The relation between traumatism and the causation of cancer cannot be established definitely from a medicolegal standpoint. This explains the divergence of opinion which often exists among experts of unquestioned scientific reputation. In this respect, the Tenth Medicolegal Congress of France (1925) re-endorsed practically without modification the report of Segond presented at the Surgical Congress in 1907, according to which the following conditions must exist to prove the causation of cancer by trauma (to conform with the employers' liability law of 1898): (1) former absolute integrity of the injured region; (2) very intense trauma leaving marks in the injured region; (3) absolute identity between the traumatized point and the site of the tumor; (4) the length of time between the trauma and the first symptoms of manifestation of the tumor should not be less than one month to six weeks; (5) continuity in the appearance of pathologic manifestations in the traumatized regions; and (6) confirmation of the malignant nature of the tumor by biopsy, whenever possible.

The injured employees were divided into five groups: (*a*) those in apparently good health injured at the level of a known healthy region (in fact, this constitutes the only group which should be given consideration if the law were rigorously applied); (*b*) those already suffering from cancer at the time of the accident in which injury occurred at a point more or less distant from the pre-existing neoplasm; (*c*) those already suffering from cancer at the time of the accident in which the injury occurred at the site of the pre-existing neoplasm; (*d*) those not definitely cancerous at the time of the accident but who were injured in a region in which a lesion predisposing to subsequent cancerous degeneration existed; and (*e*) those who became cancerous as a result of spontaneous malignant degeneration of one of the predisposing lesions of the preceding group but in which the pre-

disposing lesion itself was caused by a trauma.

After describing the type of malignant tumors which, according to the military jurisprudence of France (March 31, 1919), entitle the claimants to various compensations, the author expresses the opinion that from a clinical standpoint the relation between trauma and a malignant tumor may be of the following type: (1) trauma may occur as the occasional cause of cancer, this constituting the most disputed phase of the problem and leading to numerous errors of interpretation; (2) trauma may lead to an accidental discovery of a previously existing tumor, this being one of the most common occurrences, especially in tumors of the breast; and (3) trauma may aggravate an existing tumor.

In conclusion, the author emphasizes that in addition to legislation protecting workmen against accidental cancer caused by trauma, a protective law against occupational cancer should also be enacted. This latter is especially important since recently in certain industries several occupations were reported as etiologic agents of cancer.—*T. Leucutia.*

ICHOK, G. L'extension de la loi sur les maladies professionnelles. (Extension of the law on occupational diseases.) *Presse méd.*, April 25, 1931, *39*, 613.

The French official bulletin of October 27, 1921, published the law which for the first time applied the compensation law of April 9, 1898, to certain occupational diseases. Since then, several amendments have been made, the last that of January 1, 1931, modifying and completing the basic law.

According to the new law, the occupational diseases were divided into six groups: saturnism, hydragyrism, intoxication from tetrachlorethane, benzinism, phosphorism and intoxications caused by the action of the roentgen rays or certain radioactive substances.

For the first five groups, the duration of responsibility as determined by the statute of limitations is one year; for the last, which includes uranium and its salts, uranium X, ironium, radium and its salts, radon, polonium, thorium, mesothorium, radiothorium, thorium X, thoron and actinium, it is as follows: acute and chronic roentgen and radium dermatitis—one year; cancer of radiologists—five years; simple anemia with leucopenia provoked by radiations—one year; pernicious anemia provoked by radiations—one year; leucemia provoked by radiations—one year; bone necrosis provoked by radiations—one year. As one may note, the list is particularly disquieting and therefore the strictest precautions must be taken. This applies to the field of extraction of radioactive substances; manufacture of the derivatives of the radioactive substances; manufacture of medical apparatus for radium therapy as well as roentgen apparatus; research or measurement of radioactive substances and roentgen rays in laboratories; manufacture of chemical products and pharmaceutical radioactive substances; manufacture and application of luminescent radiferous substances; workers in clinics, medical and dental offices, dispensaries and anticancer centers who are exposed to radiation; sale and loan of radium and radioactive substances; and, finally, laborers in all industries and commerces utilizing roentgen rays and radioactive substances.—*L. Leucutia.*

IZKOVITCH, I. Röntgenologie im Dienste des Gerichts. (Roentgenology in medical service.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Nov., 1930, *42*, 664–666.

Three medical expert reports which were submitted to the courts of Haifa, Palestine, for the proof of minority of defendants are reproduced and briefly discussed. The reports were based on roentgen findings of the ossification in various bones. The point to be proved in all three instances was whether the defendant had reached his majority (18 years). The author from a study of the roentgenograms felt safe in arriving at a definite conclusion. His standpoint was accepted by the legal authorities.—*T. Leucutia.*

TAYLOR, HOWARD C., JR. The etiology of neoplasms of the breast. *Arch. Surg.*, 1930, *21*, 412–443; 597–665.

The purpose of this paper was an effort by the author to examine the evidence in support of the theory that a functional disturbance of the physiologic relationship between the ovary and the breast is an important factor in the genesis of many forms of tumor of the breast. Only a few definite studies with many scattered observations favor such a contention. Therefore, the author in his present undertaking has coordinated the recorded material into what he conceives as a logical conception.

The study of the evidence leading to the be-

lief that an endocrine disturbance is an important factor in the causation of tumors is presented as follows:

1. A consideration of the stimulus which normally produces proliferation in the breast shows that it is the ovarian secretion to which the breast cell is specifically responsive throughout life.

2. The consideration of the changing histologic structure of the breast shows that many of the pictures incident to a normal response of the parenchyma of the breast to ovarian secretion differ only slightly from that of certain neoplastic processes.

3. Attention is drawn to the fact, illustrated particularly by the work of Eugen Albrecht, that tumors resemble organs, both as regards their structure and their behavior, and very likely their origin.

4. An analogy is offered between the tumors of the breast and those of other parenchymatous organs of the reproductive system. For many of these tumors an ovarian dysfunction has been suggestive as causative; for a few it is nearly proved, and has displaced an older inflammatory theory.

5. Evidence is given to show that certain hypertrophies and hyperplasias of the breast which lie on the borderline between physiologic and neoplastic growths are probably dependent on ovarian dysfunction.

6. Evidence is given to show that certain hypertrophies in animals, and their behavior under experimental conditions, support an internal causative factor.

7. The theories of the origin of fibroma, chronic mastitis, and carcinoma are discussed.

8. The clinical study of 271 cases of mammary tumors is offered as a preliminary survey of the field of ovarian disturbance in relation to the genesis of tumors of the breast.

This article is so extensive and inclusive that it is almost impossible to give a comprehensive abstract in a limited amount of space. The author's brief conclusions are as follows.

"The parenchyma of the breast has been shown to depend on the sexual cycle for all its normal variations of structure and to be capable of rapid growth and transformations under certain physiologic conditions of ovarian activity. In this respect the breast is similar to the endometrium, the thyroid and certain ovarian structures. Pathologically, the various forms of tumor of the breast have their counterparts in the tumors of the three organs mentioned and of the prostate. What clinical observations can be collected from the literature and from this study of 271 cases indicate that etiologically the tumors of the breast, including carcinoma, are closely related to those of the endometrium, thyroid and ovary, are somewhat allied to myomas of the uterus and are in a way equivalent to tumors of the prostate. The tumors of these five organs, therefore, form a group, the etiology of whose members shows many points of mutual resemblance. To attempt to relate inflammatory accidents of lactation to cancer of the breast is to classify it etiologically with cancer of the cervix, which on both inductive and deductive grounds appears unjustifiable.

"It is possible that the contrast afforded by the causes of origin of these two common types of new growth may lead to the formulation of a general principle. Such a principle would amend the teaching that cancer results from chronic irritation by adding that the stimulus must as a rule be of the same type as that to which the particular tissue is biologically best adapted to respond with proliferation. Such a conception would appear, superficially at least, to reconcile the conflicting theories of numerous authors, who have formed their opinions of the causes of cancer from the study of the new growths of entirely different tissues. With this view it would be entirely consistent for mechanical or chemical irritants to produce cancerous changes in the protective epithelial cells covering the surface of the body and lining the walls of the intestinal tract, for an infectious agent to induce new growth in lymphoid, myeloid, or granulomatous tissue, for trauma to produce tumors by evoking the reparative function of fascial and osteogenic cells and finally for hormonal influences to be effective in producing hypertrophy, hyperplasia and neoplasms in the breast and other organs whose normal growth processes are under endocrine control."—*E. P. Pendergrass.*

ROENTGEN AND RADIUM THERAPY

Bignami, G. La radioterapia delle emopatie. (Radiotherapy of the hemopathies.) *Atti del IX Cong. Italiano di Radiol. Med.* Part I. Torino, 1930, pp. 141–314.

The article is divided into a general and a special part.

In the general part, the biological action of the roentgen rays on the blood and hemato-

poietic organs, the experimental anatomicopathologic alterations of the hematopoietic system, the modifications of the circulating blood following irradiation, the genesis of all these modifications, and finally, the influence of the intrinsic and extrinsic factors on the biological effect of the roentgen rays are discussed.

In the special part, the technique of irradiation and the results obtained in the various blood diseases are described, numerous case reports, richly illustrated with drawings and summarizing tables, being included. For the sake of convenience the blood diseases are arranged in the following groups: (1) leucemia (myeloid, lymphatic and aleucemic, acute and chronic); (2) Vaquez' disease; (3) aplastic anemia; (4) pernicious anemia; (5) granuloma malignum; (6) Gaucher's disease; (7) Mikulicz's syndrome; (8) chloroma; (9) myeloma; (10) lymphosarcoma and lymphosarcomatosis; (11) systemic neoplasia of the lymphatic glands; (12) primitive splenomegaly (Banti, Gamna, splenomegalic hemolytic icterus); (13) hemorrhagic diathesis. Five colored plates (10 figures) showing the most typical forms of blood pictures are appended.—*T. Leucutia.*

SICILIANO, LUIGI. Commenti e problemi intorno alla radioterapia delle malattie del sangue. (Comments and problems of radiotherapy of blood diseases.) *Atti del IX Cong. Italiano di Radiol. Med.* Part I. Torino, 1930, pp. 315–343.

Based on the more recent publications in the medical literature and on his own personal experience, the author deals extensively with several important problems of the roentgen therapy of the blood diseases. Chief among these are the formation of the cell elements of the blood and the reciprocal relation of the white and red cells of the hematopoietic system; the modifications of the blood formula following immediately or at a later time the application of irradiations; the relative roentgen susceptibility of the white and red elements; the phenomenon of deficiency of the circulating blood depending on the amount of radiation administered; the indirect as well as the distant effect of the roentgen rays; the question of stimulating doses; the importance of the irradiation of the spleen and the effect of the various techniques; and finally, the varying radiosensitivity of other affections of the lymphatic apparatus.—*T. Leucutia.*

FERRATA, ADOLFO. Emopatie e raggi Roentgen. (Hemopathies and roentgen rays.) *Atti del IX Cong. Italiano di Radiol. Med.* Part I. Torino, 1930, pp. 345–352.

In briefly summarizing the knowledge in such a vast and difficult field, the author states that two systemic hemopathies are efficaciously treated by roentgen therapy: the leucemias and the malignant granulomata. Next in line, one may mention the tumors of the lymphatic glands, such as lymphosarcoma and the lymphadenoid hemosarcomas of systemic aleucemic type. In the other hemopathies (pernicious anemia, hemorrhagic diathesis, chloroma, myeloma) the curative effect of the roentgen rays is not so certain, the effect being of only temporary duration, and a relief of the hemorrhagic syndrome (by irradiation of the spleen) being the only positive result. In advanced primary and secondary anemias (pernicious or pernicious-like anemias, hemorrhagic icterus, symptomatic anemia, chlorosis, etc.) small doses of roentgen rays may lead, as proved by numerous experiments, to stimulation of the hematopoiesis.

The conclusion is reached that roentgen therapy forms a very valuable adjunct in the treatment of various forms of blood diseases, this necessitating a close cooperation between roentgenologist and internist, both as regards the diagnosis and treatment.—*T. Leucutia.*

GURD, FRASER B. Modern methods in the treatment of carcinoma. *Canad. M. Ass. J.*, Dec., 1930, *23*, 784–792.

The author discusses the treatment of carcinoma in a general manner as carried out at the different European centers. The organization of the Radiumhemment at Stockholm is rather minutely described and the methods of treatment briefly discussed. Radium element is used exclusively instead of emanation. Roentgen therapy is employed very extensively both as a preoperative and postoperative measure, particularly in cases of breast carcinoma and is used before radium in extensive cases of faucial carcinoma, especially those associated with inflammation. Electrocoagulation is combined with irradiation in cases of carcinoma of the vulva. The routine in carcinoma of the mouth is usually roentgen therapy, electrocoagulation and introduction of radium tubes.

Breast carcinoma is treated at Stockholm by preoperative roentgen therapy, through five

portals. Mammectomy is then performed in the operable cases and is followed by postoperative irradiation through three portals. This technique is compared with Keynes' method of long-continued interstitial irradiation of the breast and lymph drainage employed at the St. Bartholomew's Hospital in London, and Cade's technique at Westminster in London, where in addition to long interstitial irradiation, surface application of radium is employed.

They have not employed radium in the treatment of rectal carcinoma at Stockholm. Pre- and postoperative deep roentgen therapy is given in rectal carcinoma. They are unwilling to express an opinion of the value of irradiation in the treatment of gastric and esophageal carcinoma. Gask, at St. Bartholomew's Hospital and Cade, at Westminster, do not employ electrocoagulation in treatment of carcinoma of the tongue. Gask employs interstitial irradiation entirely. Cade combines distant radium application, interstitial irradiation and block dissection of the neck, when necessary, with postoperative radium at a distance. The radium bomb or "telecurie therapy" as employed at the Radiumhemmet, at the Curie Institute and Westminster Hospital, is briefly discussed.—*J. H. Vastine.*

Santoro, Angelo. Quello che ho visto ed udito a Parigi negli Istituti di Radiumterapia. (What I saw and heard at Paris in the institutes of radium therapy.) *Arch. di radiol.*, 1930, *6*, 855–869.

The author recently visited all the important institues and hospitals in Paris where radium treatment is given. These institutes have generous supplies of radium available. The principle used in irradiation of tumors is that of a minimum amount of radioactive substance, maximum filtration and long time of exposure. Long exposure permits of all the cells being acted on during their most active phase when they are most sensitive to irradiation. The maximum filtration is necessary in order to protect the normal tissues.

It is quite generally agreed that cancer of the body of the uterus should be operated on, but in cancer of the cervix radium therapy has given the best results. Surgeons and radiotherapists still disagree as to the best treatment of the early stage, as both methods give very good results, particularly since the use of the Mikulicz drain has enormously improved the statistics for Wertheim's operation. The statistics for radium therapy show 80 per cent good results when the right technique is used and sufficient dosage given. The superiority of radium therapy is more generally admitted when the process has extended to the glands of the parametrium and it is universally admitted when the uterus is blocked and immovable. Denabias no longer introduces the radium into the cervical canal and cavity of the uterus but uses a circular pessary containing radium applied around the cervix and a T pessary to hold the radioactive substance in contact with the anterior part of the cervix. The treatment should be continued not less than fifteen to twenty days or possibly twenty-five days if microscopic examination shows few mitoses. There are two methods of treating the affected lymphatics: either by laparotomy and applying the radium to the lymphatic trunks or applying it externally by means of a Columbia paste apparatus. Radium treatment of carcinoma of the cervix has been used successfully even in pregnant women; experience has shown that the cervix may be sterilized with radium without injuring the fetus.

Cancer of the vulva has been successfully treated with radium by fixation with needles. Good results are reported in 50 to 80 per cent of cases of cancer of the vagina. Radium should not be used for preoperative treatment but gives very good results as a postoperative treatment.

There is difference of opinion in regard to the use of radium for cancer of the breast. Denabias divides them into two classes: cylindrical celled epitheliomas and gland epitheliomas. He says the former should be treated surgically but the latter are amenable to radium treatment. When the glands are involved there is recurrence in 45 per cent of the cases after surgery and in not more than 5 per cent after radium. The radium is applied by means of Columbia paste containing 100–120 mg. radium and left on for twenty-one days.

Radium may be applied in cancer of the bladder by cystostomy or with a rubber catheter. The latter technique is preferable unless operation is required for some other purpose.

Cancer of the prostate is hard to treat. Needles are inserted in the tumor either through a large incision in the perineum or by puncturing the perineum with a trocar. Radium has been used successfully in some cases of cancer of the penis but as a rule surgery is to be preferred.

Radium has been successful in 60–70 per cent of cancers of the lip when the glands are not infiltrated. Some cases of cancer of the tongue have been treated successfully by radium needles, though this is a very difficult form of cancer to cure by any method. Fixation with needles has been used in a few cases of cancer of the pharynx but generally the radium is applied externally with a Columbia paste apparatus or at a distance. The results are encouraging. Cancer of the esophagus so far has not given good results. Cancer of the rectum is also difficult or even impossible to cure with any method but radium gives good palliative results.

Skin epitheliomas can be cured with a small amount of radium and a long exposure time. Good results have been reported from radium treatment of brain tumors, chiefly by external application but in some cases after craniotomy. Radium has also been tried in tumors of the lungs and pleura and some good results have been obtained using the same method as in cancer of the breast.—*Audrey G. Morgan.*

HERENDEEN, RALPH E. Results in the roentgen-ray therapy of giant-cell tumors of bone. *Ann. Surg.*, Jan., 1931, *93*, 398–411.

The author believes that at times there appears to be a tumor which possesses some of the roentgenographic and histological features of giant cell tumor, but potentially malignant as shown by subsequent events. He reports a case of giant cell tumor which was regarded as typical by Kolodny from the roentgenographic standpoint but which later developed metastasis in various bones of the body and continued to do so at the time this article was prepared. These metastases appeared from four to eight months apart and following roentgen irradiation they promptly disappeared and did not recur.

The author believes that a larger percentage of giant cell tumors recur after curettage than is commonly supposed. The Memorial Hospital reports 25 per cent of recurrence after curettage.

Patients with giant cell tumor of the lower end of the femur are the most important from an economic standpoint and the most satisfactory group. Frequently the surgical results here are in comparison quite unsatisfactory due to the deformity of the joint surface and the limitation of motion following operative interference.

The treatment used "varies with the case." Few of the tumors respond alike to the same dose of roentgen rays. The author maintains that best results are obtained by using relatively small doses and judging further treatment by examining the part, and inspection and comparison of the roentgenograms obtained from time to time. His factors are, 140 kv., 4 ma., 4 mm. Al filter, 12-inch target skin distance and from 12–15 minutes' exposure, a series of treatment consisting of 3 treatments, from three days to one week apart and an average of 8 to 10 treatments given. The portals consist of the external, anterior and internal surfaces.

Seven cases of giant cell tumors of bone which have been treated by roentgen rays are reported with but one recurrence which later was treated and disappeared. Very good case histories and roentgenograms accompany these reports.—*F. K. Alexander.*

QUICK, DOUGLAS. Interstitial radiation in metastatic cervical nodes of epidermoid carcinoma. *Ann. Surg.*, Jan., 1931, *93*, 380–390.

The author believes that up to a certain point cervical nodes form a conservative function, even though involved, and hence should not be disturbed if avoidable, particularly in the presence of an active primary growth. Thus the premise that extension is by embolism rather than by permeation has been accepted by this writer. For these reasons routine dissection, either unilateral or bilateral, have not been resorted to.

Lymph node areas of the neck in every case of intraoral cancer are irradiated as promptly as possible, following which unilateral neck dissections under local anesthesia are done in cases of adult type epidermoid carcinoma presenting clinically involved unilateral nodes. The primary growth must be controlled or present favorable evidence of that result and the involved nodes must present intact capsules. Bilateral involvement and perforation of the node capsule are considered an indication of inoperability.

Martin and Quimby have shown that in order to produce complete regression of the adult types of epidermoid carcinoma an intensity of from 7–10 skin erythema doses is necessary and with the cellular undifferentiated epidermoid carcinoma, the minimal essential intensity varies from 3–5 skin erythema doses.

The question arises as how to best supplement the external radiation in the cases called inoperable.

The author prefers implantation. The implantation is done under local anesthesia, using the least possible dissection. Maintenance of the blood supply is essential for the tissue to stand the resulting large amount of skin erythema doses to be given. Careful exposure lends accuracy to implantation and lessens the danger of injury to adjacent vessels and nerves. After emanation tubes have been implanted the wound is carefully closed with careful approximation of skin and muscle. If the external dosage has been carried out within a brief period—a week—then the exposure and implantation may be carried out at once and primary healing obtained before the maximum skin reaction has been reached.

In view of the fact that a localized metastatic mass may be completely controlled by this method of irradiation, operative surgery is relieved of the necessity for attempting extensive operative procedures. In some, at least, of the metastatic cases which may be classed as surgically operable, the method has made a very favorable impression and may with added experience afford a substitute for complete unilateral dissection.—*F. K. Alexander.*

Santoro, Angelo. La radiumterapia del cancro della bocca. (Radium therapy of cancer of the mouth.) *Radiol. med.*, Jan., 1931, *18*, 115–128.

Histories are given of 18 cases of cancer of the mouth treated with radium at the Institute of Medical Radiology of the University of Rome. The results show 61 per cent of clinical cures, the longest period of cure being a year and eight months and the shortest four months. —*Audrey G. Morgan.*

MacFee, William F. Concealed cancer of the tongue. *Ann. Surg.*, Feb., 1931, *93*, 481–488.

In spite of the fact that the tongue is an accessible organ 20 per cent of the cases of cancer of the tongue are anatomically situated in such a way that they escape early detection.

The clinical types of cancer of the tongue which escape detection are of two kinds. The first is located far back on the tongue, at the base of the pharyngeal or tonsillar sinus, at the lingual attachment of the glosso-palatine arch, in the vallecula, or at the glosso-epiglottic fold. The other type escapes detection because it is almost completely buried in the substance of the tongue. This type is nearly always in the posterior half or two-thirds and is found most often on the inferior surface of the oral portion of the tongue where its mucous membrane reflects into the floor of the mouth. There is usually a slight dimple or pucker in the mucous membrane over the most superficial part of the tumor; there may or may not be a loss of epithelium.

The palpating finger and the laryngoscopic mirror are the two methods best used to locate these lesions. Pain is inconstant and usually absent at first, and in the early cancers in the posterior half of the tongue a referred pain to the ear via the tympanic branch of the glossopharyngeal. An awkwardness in movements of the tongue and a queer unnatural sensation in the involved side of the tongue are other common symptoms.

The author reports two case histories bearing out his observations.—*F. K. Alexander.*

Ahlbom, Hugo. Castration by Roentgen rays as an auxiliary treatment in the radiotherapy of cancer mammae at Radiumhemmet, Stockholm. *Acta radiol.*, Dec. 31, 1930, *11*, 614–635.

After a brief historical review of the subject, the author discusses the theoretical principles of castration in cancer of the breast. He then gives a statistical account of 163 cases of cancer of the breast castrated by roentgen rays at the Radiumhemmet from 1922–1928. In a few of the cases the tumor was not irradiated directly; in the other cases the castration treatment was combined with roentgen or radium irradiation of the tumors or metastases. In the cases treated by castration alone, all of which were in an advanced stage, the treatment had no effect. The results obtained in the cases treated by castration and irradiation of the tumor are compared with those obtained by irradiation of the tumor alone without castration. The comparison shows that the irradiation of the ovaries did not prolong life. The group treated by castration showed slightly better results than the non-castrated group with regard to rate and duration of improvement in patients more than forty-five years of age, after excluding from both groups of cases the patients whose general condition was seriously impaired by the cancer.

The author does not think that definite conclusions can as yet be drawn in regard to the value of the treatment. The material includes very few of the cases in which good results are to be hoped for, that is, cases in young women still menstruating in whom the disease has not spread beyond the first lymphatic glands. There is no evidence that the castration treatment has any bad effect.—*Audrey G. Morgan.*

PFAHLER, GEORGE E., and PARRY, LEO D. Roentgen therapy in carcinoma of the breast; a statistical study of 977 private cases. *Ann. Surg.*, Jan., 1931, *93*, 412–427.

This is a tabular and statistical study and is not suitable for abstracting.—*F. K. Alexander.*

STIEVE, H. Unweltbedingte, nicht durch Röntgenstrahlen veranlasste Keimdrüsenschadigungen. (External injuries of the genital glands not caused by roentgen rays.) *Strahlentherapie*, 1930, *37*, 491–510

The author discusses the injuries of the sex glands and cells brought about by various external agencies such as toxins and trauma, and gives histological illustrations of sex glands that have suffered such injuries. Such injuries, acting through the body as a whole may destroy maturing sex cells, leaving only the resting ones. If the injury keeps up long enough even these may be destroyed and the animal become permanently infertile. The female becomes sterile easier than the male but it is only in very severe cases that all the reproductive cells are destroyed. In the majority of cases the spermatogonia in the testicles and the primordial follicles in the ovaries remain unchanged and as soon as the general injury is removed or overcome they develop in the usual way. The cells that now mature are normal and give normal offspring, so the reproductive cells are either destroyed entirely and produce no offspring or they produce normal young. There is no evidence that injured reproductive cells develop and produce malformed offspring. The author believes that the same thing holds true of injury of the sex glands by roentgen rays. He argues that if all the injuries that might affect the sex glands of an animal also affected the resting reproductive cells so that they might develop later and produce malformed offspring there would by this time be no normal individuals but only crippled and deformed ones.—*Audrey G. Morgan.*

PORTMANN, U. V. Radiation therapy of tumors of the genito-urinary tract. *Radiology*, Nov., 1930, *15*, 542–543.

The radiosensitivity of bladder tumors will depend upon their degree of differentiation—the less differentiated types will require very large doses to accomplish any benefit. These cannot be administered by roentgen rays alone, but require the combination of radium and roentgen therapy, and this, of course, is a surgical procedure. It is probable that operation alone can cure only those cases in which the growth is entirely and completely localized, or in which a complete cystectomy can be performed. Necessarily there is a very high mortality rate from such a procedure.

When the author first began to treat bladder tumors by deep therapy he was very much discouraged, because most of the cases that were referred to him were sent because of recurrence following operation. In the light of his present view of bladder neoplasms, good results could not have been expected, because the surgical procedure in itself would have changed the entire situation so far as the blood supply was concerned, as well as probably changing the characteristics of the growth, so that it became less differentiated. He believes that if bladder malignancies be looked upon as all being of the papillary type, with greater or less differentiation, except an occasional case of epidermoid carcinoma, and therapeutic procedures be planned according to the type of papillary formation, roentgenologists will be very much better satisfied with the results of their treatment.—*J. D. Camp.*

ACTION OF ROENTGEN RAYS AND RADIUM ON THE HEART AND LUNGS

EXPERIMENTAL DATA AND CLINICAL RADIOTHERAPY

BY

A. U. DESJARDINS

MAYO CLINIC

ROCHESTER, MINNESOTA

SECTION ONE

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PREFACE

Strange as it may seem to the initiated, the existence of a scientific foundation for radiotherapy is even now being questioned. In a recent editorial in the Lancet* it was stated that "there is still an uncomfortable amount of truth in the gibe that the whole of radiology in its radiotherapeutic aspect lacks scientific basis and rests largely on an empirical footing." Casual reading of contemporary medical records bearing on the action of roentgen rays and radium often gives the impression that little is known concerning such action, in spite of the fact that, as far as many phases of the subject are concerned, more or less substantial or conclusive experimental data are available to indicate, or to clearly establish, the nature of such action. In some cases, indeed, the experimental indications are absolute. In other cases adequate experimental evidence may be lacking, but the clinical data may be sufficient to indicate the probable effect of irradiation. It must be admitted that many problems relating to radiotherapy are still the subject of controversy and that the large number of experiments which have been made have yielded only partial answers to many questions. Nevertheless, the experimental facts already established are sufficiently numerous to provide an adequate, although incomplete, scientific background. Unfortunately, the evidence furnished by experiments on animals and by clinical reports has never been brought together, analyzed, and correlated, and much of it has been lying on library shelves, buried in medical journals which are seldom read. Colwell and Russ and a few others have, it is true, examined some of this material and have made valuable deductions, but a thorough analysis and appraisal have never been undertaken.

Before the action of roentgen rays and radium on pathologic lesions can be understood, it is essential to know the action of such rays on normal cells and tissues. The object of this work is to bring together the available experimental and clinical evidence and to subject this material to close scrutiny, with a view to extracting from it the essential information about the effects of roentgen rays and radium on normal tissues and organs. The method adopted has been to prepare a careful and complete abstract of each original report, as published by the experimenters themselves, including every item of essential information therein contained. Every effort has been made to preserve as much as possible the meaning of the authors of such reports, even to the point of preserving ambiguous statements when such statements were present. These abstracts have been arranged in chronologic order to facilitate reference and enable the reader to follow the historical development of the subject. The experiments with roentgen rays have been grouped separately from those with radium. These two groups of experimental reports have then been subjected to critical analysis, and this follows the experimental reports themselves. The analysis, in turn, is followed by the clinical considerations, in which is taken up the therapeutic application of roentgen rays and radium to every disease by which the particular tissues or organs are affected. Finally, all the data, experimental and clinical, are correlated and summed up.

* Lancet, 1931, *1*, 141.

Although the greatest care has been taken to make this study as complete and as thorough as possible, I am conscious that errors, discrepancies, and oversights must have occurred. Certain experiments may unwittingly have been omitted. The opinions expressed are my own, and for these I hold myself responsible. It is probable that, as time goes on and as fresh material becomes available, some of the deductions and conclusions may have to be modified. As far as the clinical considerations are concerned, it has been impossible to mention every report which has appeared in the literature, because this would have involved long lists of names which must serve only to tax the patience of the reader. In dealing with this phase of the subject, I have taken pains to include every author of importance and to give to each country due representation in proportion to the number of communications emanating from it. In this way, it will serve to indicate the country in which certain phases of radiotherapy have been most highly developed. The bibliography is substantially complete, although a few items which could not be procured have been omitted. I will appreciate having my attention drawn to any significant omission.

Rochester, Minnesota,
March, 1931.

ACTION OF ROENTGEN RAYS AND RADIUM ON THE HEART AND LUNGS

HEART

General Considerations

The specific sensitiveness of the heart to roentgen and radium rays has always been regarded as slight in comparison with that of many other organs and structures. Little evidence that ordinary therapeutic doses of radiation exert an injurious effect on the heart has ever been adduced, and such evidence as has been submitted has been of uncertain quality. A review of the animal experiments, the object of which was to test the influence of radiation on the heart, will be interesting if only because they indicate the conditions under which the heart may be affected by irradiation, as well as the direct and indirect effects of such exposure. Some of the early experimenters, such as Heineke, and Krause and Ziegler, made only casual mention of the negative action of roentgen or radium rays on the heart, because their attention was directed chiefly to the lymphatic structures and lymphoid tissues generally. They often failed to examine the heart, and for this reason, their experiments will be described elsewhere.

Animal Experiments

Roentgen Rays. Sabrazès and Rivière (1897), without describing their experiments, stated that tracings of the heart of a frog exposed to an intense source of roentgen rays showed that the cardiac rhythm remained unaffected, even by exposure for one hour.

Allen (1903) investigated the effect of roentgen rays on the isolated heart[1] of ten frogs and one tortoise. The heart of one frog was excised, kept moist with normal salt solution, beating eighteen times per minute, and was exposed to the rays for eleven minutes at a distance of 25 centimeters. The heart rate was still eighteen after irradiation for nine minutes, but after ten and one-half minutes only faint contraction could be seen. The pulsation ceased altogether after irradiation for eleven minutes and did not recover during the ensuing hour. The heart of a second frog killed by electrocution, and of a third killed with chloroform, were excised and kept moist with salt solution. One organ beat strongly at the rate of thirty-two, and the other beat weakly at the rate of twenty-eight, pulsations per minute. The first of these two hearts ceased beating after irradiation for one minute and ten seconds, and the second after irradiation for one minute, at a distance of 25 centimeters from the anode of the tube. Neither organ recovered during the ensuing half hour.

After pithing the brain and spinal cord of seven frogs and one tortoise, the thorax and pericardium were opened and the heart was made to write kymographic tracings in the ordinary way. The entire animal was protected from the rays by sheet lead, except for an opening just sufficient to allow the rays to reach the auricles and ventricles. The exposures varied between five and thirty minutes. In no case was any effect noted with less than three minutes', and usually with less than ten minutes', exposure. Seventeen tracings were made, four of which showed no change. The other thirteen all showed a diminished amplitude of contraction, and in five instances both the amplitude and the rate of contraction diminished after irradiation.

[1] The heart was placed on an insulated support, as nearly as possible in line with the angle of deflection of the cathode stream. Between the tube and the heart was a grounded aluminium filter (thickness not specified), the wire to ground and the two feed wires to the tube being as remote as possible from the heart, so as to reduce to a minimum the magnetic field around the tube. The generating apparatus consisted of a 12-inch Heinze high-potential coil, and the quality of the rays was such as to clearly show the bones of the wrist. Changes of air, temperature, light, and moisture were avoided as much as possible.

Fresh, actively beating hearts resisted the influence of the rays, while inhibition was best seen when the heart was tired or overtaxed. Attention was drawn to the lack of control animals and to possible variations in the temperature of the air as possible defects in the experiments. Allen concluded that roentgen rays tend to inhibit cardiac function in cold-blooded animals.

Warren and Whipple (1922) tested the comparative sensitiveness of the thoracic and abdominal organs to roentgen rays by exposing the thorax and abdomen of three adult dogs, and later the abdomen only of two of these dogs, to from 350 to 450 milliampere-minutes of rays of moderate quality. A detailed description of these experiments is given elsewhere. Diarrhea, vomiting and prostration; marked degeneration, hemorrhagic extravasation, edema, and desquamation of the epithelium and mucosa of the small intestine; atrophy of the spleen, and moderate destruction of lymphocytes in the lymph nodes, intestinal follicles, and bone marrow were noted in all the animals subjected to abdominal irradiation. But clinical or pathologic disturbances were not found in the heart of animals irradiated over the thorax.

Gordon, Strong and Emery (1924) investigated the functional and organic effects on the heart of exposing the precordium of sixteen rabbits, weighing from 1.8 to 3.8 kg., to the direct action of large single, moderate repeated, or small doses of roentgen rays repeated at frequent intervals over a period of several months.[2] Each rabbit was placed on its back on an animal board and firmly held in place. Except for the area exposed, the body was protected from the rays by a sheet of lead.[2] The precordial area exposed to the rays measured 2.5 by 3.0 centimeters. In the rabbits used to study the effect of indirect irradiation the precordial area was shielded with lead and the lower part of the abdomen was uncovered. Electrocardiographic tracings and roentgenograms at a uniform distance of 4 feet were made before, and at frequent intervals during and after, irradiation to determine any change in the size and function of the heart. The cardiac shadow was outlined on the roentgenograms and a silhouette was traced on smooth white paper. The silhouettes were cut and weighed, the weight being accurate within 1 milligram. When the film gave evidence of distortion it was discarded.

The precordium of one rabbit was irradiated for 375 milliampere-minutes in one session, and the animal died twelve hours later. The precordium of five rabbits was irradiated for 75 milliampere-minutes in one session, and the animals died 18 days, 12 hours, 10 hours, 12 hours, and 12 hours, respectively, after exposure. During the interval the weight of the animals did not vary, and signs of toxicity were not apparent at any time. The precordium of one rabbit was irradiated for 225 milliampere-minutes in one session. Symptoms of illness, said to represent intercurrent infection, appeared, and the animal died five days after exposure to the rays; its weight had remained stationary. The precordium of one rabbit received a total of 1000 milliampere-minutes at the rate of 150 milliampere-minutes every three weeks; the animal died six months after the first, and one month after the last, irradiation. The precordium of one rabbit received a total of 1000 milliampere-minutes at the rate of 75 milliampere-minutes once a week; the animal died six months after the first, and five weeks after the last, irradiation. The weight of each of these two rabbits diminished 0.1 kg. during the interval.

The precordium of one rabbit received a total of 775 milliampere-minutes at the rate of 25 milliampere-minutes twice a week; signs of toxicity did not appear at any time, but the animal died six and one-half months after the first, and five weeks after the last, irradiation; its weight had increased 0.4 kg. during the interval. The precordium of one rabbit received a total of 960 milliampere-minutes at the rate of 40 milliampere-minutes twice a week; manifestations of toxicity did not appear at any time, but the animal died five months after the first, and two weeks after the last, irradiation; its weight had diminished 0.1 kg. during the

[2] Beyond mention of the number of milliampere-minutes of irradiation, the other conditions of irradiation, the physical quantity and quality of the rays, the focal-skin distance, etc., were not specified.

interval. The precordium of one rabbit received a total of 525 milliampere-minutes at the rate of 225 milliampere-minutes every three weeks; symptoms of illness, possibly resulting from an infected foot and accidental exposure of the abdomen to roentgen rays, were featured by severe diarrhea, and death ensued thirty-six days after the first, and fourteen days after the last, irradiation. The weight had diminished 1.0 kg. during the interval.

In order to determine any indirect effect on the heart, the precordium of one rabbit received a total of 750 milliampere-minutes at the rate of 75 milliampere-minutes once a week. Symptoms of illness were slight, the weight diminished 0.5 kg., and the animal died from pulmonary complications four and one-half months after the first, and five weeks after the last, irradiation. The precordium of one rabbit received a total of 600 milliampere-minutes at the rate of 300 milliampere-minutes once a month. Symptoms of illness were slight, the weight remained stationary, and this animal also died from pulmonary complications six weeks after the first, and three weeks after the last, irradiation. The precordium of one rabbit was irradiated for 900 milliampere-minutes at the rate of 300 milliampere-minutes once a month. Toxic manifestations developed, and the animal died four months after the first, and seven weeks after the last irradiation; its weight had decreased 0.5 kg. during the interval. The precordium of one rabbit received a total of 150 milliampere-minutes at the rate of 50 milliampere-minutes once a week. Slight symptoms of illness from an intercurrent infection appeared, the weight diminished 0.7 kg., and death ensued fifteen days after the first, and one day after the last, irradiation.

The abdomen of seven additional rabbits was irradiated at one time for 150, 300, 300, 225, 300, 300, and 225 milliampere-minutes, respectively. Four animals did not exhibit systemic reaction of any kind, and three others showed some degree of reaction in the form of diarrhea. The weight of five animals apparently did not vary.[3] Of the two remaining rabbits the weight diminished 0.1 kg. in one and increased 0.1 kg. in the other. One animal which had not given any signs of reaction was killed eighteen days after irradiation; three rabbits died or were killed one day after irradiation;[4] two died or were killed seven days after irradiation, and one died or was killed twenty-one days after irradiation.

In only one rabbit subjected to precordial irradiation the electrocardiograms showed ventricular extrasystoles after a total irradiation of two hours and five minutes, at the rate of fifteen minutes weekly; the extrasystoles ceased when irradiation was stopped. All the other animals failed to show the slightest variation in cardiac function. Nor did any of the rabbits exhibit an appreciable alteration in the size of the heart. With the exception of those in which gastrointestinal disturbance, loss of weight, or infections developed, all the animals remained in good health and did not give evidence of myocardial insufficiency. All but the five rabbits that died were killed with ether. At necropsy the heart did not show constant pathologic changes. A few whitish spots on the myocardium and clumps of fibrin in the pericardium were found in two rabbits. Otherwise, the gross appearance of the heart was always negative. Histologically, small areas of necrosis or fatty infiltration were found in several instances; such findings were not characteristic of myocardial degeneration, but suggested the effect produced by different infections, intoxications and nutritional disturbances.

Roffo (1924) tested the effect of roentgen rays on *in vitro* cultures of embryonal tissue from the heart. The first cultures exposed to the rays grew better than had been anticipated; the rays apparently did not affect the development of such tissue. The heart of chick embryos and chicken plasma with Ringer's solution were used, four slices per culture, each with a control, and the remnants of tissue were treated in the same manner; each pair of culture capsules were irradiated in such a way that it was possible to ascertain which grew the fastest. In order to determine the effect more accurately, the tissue was irradiated *in vitro* immediately after it had been placed in plasma and again after twelve hours of culture, when a zone of growth was perceptible.

[3] The weight of three of these animals before and after irradiation was not given.

[4] The data given in the text and in the table do not agree.

In the first experiment the heart of fourteen chick embryos nine days old was exposed to high-voltage roentgen rays[5] for from ten to sixty minutes, representing from one-third to twice the human erythema dose. Two control preparations were not exposed to the rays. The irradiated preparations developed as well and as rapidly as the controls. In a second experiment the heart of twelve chick embryos eight days old was exposed to roentgen rays[6] of short wave-length for from seventy to 120 minutes, representing from 1.36 to 2.36 of the human erythema dose. Two other preparations were not irradiated to serve as controls. No difference in development between the irradiated and control preparations could be observed. In a third experiment the heart of nine chick embryos eight days old was exposed to roentgen rays, under the same conditions as in the preceding experiment, for from 240 to 220 minutes, representing from 2.76 to 4.32 of the human erythema dose. Two other preparations were left unirradiated to serve as controls. Again no difference between the irradiated and control preparations was noted. In a fourth experiment the heart of eight chick embryos nine days old was exposed to unfiltered roentgen rays[7] of short wave-length for from ten to twenty-five minutes, representing one and one-half to two and one-half times the human erythema dose. Two other preparations were left unirradiated to serve as controls. The results were completely negative. To exclude the possibility that resistance to radiation might be due to absorption of the rays by the glass overlying the tissues and plasma, this absorption was measured by physical means and was found equal to approximately 3 millimeters of aluminium; this reduced the surface dose to 6 H for soft rays and could not vitiate the results to an appreciable degree. Doses of roentgen rays[8] up to seven times that which was necessary to produce cutaneous erythema were employed in additional experiments without any effect on the development or multiplication of the cells.

Thinking that these negative results might be due to lack of absorption of hard rays, similar experiments were carried out with unfiltered rays,[9] but the development of heart tissue *in vitro* remained unaffected, even when subjected to the rays for three hours. Assuming that the failure to influence the cultures might be related to insufficient absorption because of the thinness of the preparations, some were irradiated at a longer focal-tissue distance, but again without effect. To test the relative vulnerability or radiosensitiveness of embryonal and actively proliferating cells, other experiments were conducted on recently planted cultures of heart tissue before proliferation had started, and also on two-hour cultures which already had a concentric zone of newly formed cells. The results were the same as in the previous experiments. Roffo concluded that heart muscle is comparatively insensitive to radiation, as the experiments of Gordon, Strong, and Emery had previously shown, but that the medium in which the heart muscle cells grew may have altered their reactivity. He cited the experiments of Jolly on the thymus to support the idea that tissues isolated from the organism do not react in the same way, probably because the physico-chemical factors regulating the metabolism of the protoplasm influences the biology of the cells and hence their radio-sensitiveness. Roffo pointed out, however, that in his experiments the vitality of the tissues was not only preserved, but increased, as shown by the cellular multiplication, and yet the cardiac tissue proved resistant to the rays.

Swann (1924) investigated the immediate, functional effect of roentgen rays on various tissues and organs by exposing, usually, the entire body of an unspecified number of cats, guinea pigs, and rabbits to unfiltered rays of medium quality[10] for varying periods. A marked

[5] Rays generated at 200 kilovolts, filtered through 0.8 mm. of copper, and 1 mm. of aluminium, at a focal-skin distance of 23 cm.; with 5 ma. of current.

[6] Rays generated at 200 kilovolts, filtered through 0.8 mm. of copper and 1 mm. of aluminium, at a focal-skin distance of 30 cm., with 5 ma. of current.

[7] Rays generated at 200 kilovolts, unfiltered, at a focal-skin distance of 23 cm.; with 5 ma. of current.

[8] The wave-length of the rays was given as 0.6 Å.

[9] The wave-length of the rays varied between 0.14 and 0.16 Å. It is obvious that Roffo transposed the wave-length of the rays in the different experiments or did not realize that rays of from 0.14 to 0.16 Å are shorter in wave-length than rays of 0.6 Å.

[10] The roentgen rays were generated by gas tubes of the same make, operated at a potential equivalent to a point-plate spark-gap of from 4 to 7 inches; the focal-skin distance varied between 6 and 10 inches; and the intensity of the current, between 1 and 2 ma.

and progressive fall in blood pressure, recorded continuously by a mercurial manometer, was noted after three or four fifteen-minute exposures of the thorax and abdomen, broken by short intervals of rest. In several experiments the animal died after the second exposure. Death was never due to respiratory failure, because life could not be prolonged by artificial respiration, and respiration continued for some time after the heart had ceased to beat. In every instance the immediate cause of death was cardiac failure. No such effects were observed in any of the control experiments. The early fall in blood pressure did not seem to be due to a diminution in cardiac output, since the heart appeared to beat more vigorously than the normal organ. Respiration increased in depth and frequency at first, but later marked respiratory depression occurred. On investigating the possibility of a reflex action of the rays on the sensory nerve endings, Swann found that stronger and stronger faradic currents were required to produce the same increase in respiration which, after prolonged exposure, was always depressed.

To study the action of irradiation on the isolated heart of frogs, the animal was completely pithed without bleeding and a small incision made on the ventral surface to allow of a record being taken by the suspension method after cutting the suspensory ligament. The heart was perfused with oxygenated Ringer's solution at a temperature of from 37 to 39° Centigrade, and was exposed to roentgen rays[11] for from five to thirty-one minutes. These experiments were uniformly negative. Swann stated that "the frog's heart is notoriously unresponsive to extraneous conditions." The heart of rabbits, however, behaved quite differently. These hearts were perfused by the method of Langendorff with oxygenated Ringer's solution, the temperature of which was carefully regulated. A filter was placed in the cannula tied into the aorta to prevent blocking of the coronary vessels, because irradiation caused the heart to die in systole, and this was thought to be due to plugging of these vessels by foreign matter or to muscular contraction. In some experiments the first effect of roentgen rays was to increase the amplitude of contraction, and diastole was sometimes lengthened. After irradiation for more than fifteen minutes, the cardiac contractions diminished without any rise in tone. When the heart was exposed to the rays for much longer periods, the tone of the muscle increased slowly, and this became progressively more marked until, after about three hours of interrupted irradiation, the heart ceased to beat in systole. Curiously enough, the flow through the coronary vessels increased instead of decreased. Fibrillary twitching of the organ did not occur. Constriction of the bronchial muscles, tonic contraction of the uterus, and increase in the tone of the intestine also were observed. Swann also found that the sympathetic nerves became more sensitive after short exposures, and depressed after prolonged exposures, to roentgen rays, but did not attempt to interpret his findings.

Davis (1924) undertook to investigate, in an unstated number of rabbits and dogs,[12] the action of roentgen rays on the normal lung and the character of such action. The animals were carefully selected, and the controls were kept in the same surroundings as the experimental subjects. Sufficient time was allowed before the experiments to exclude distemper. The blood and urine were not examined, but a clinical record of respiratory symptoms, loss of weight, and other disturbances was kept. From 0.016 to 0.032 gram of morphine was used to keep the dogs quiet during irradiation. In some of the experiments the entire thorax was exposed to the rays and other animals were used as controls. In most of the experiments, however, only the right half of the thorax was irradiated and the left lung of the same animal served as control. The dose of roentgen rays at each exposure, and the number and time of such exposures, were not given for all the animals. Complete data were furnished for only two rabbits and one dog, but the changes observed in these three animals were described as representative of all the animals. In all the animals the dose of roentgen rays was sufficient

[11] The rays were generated at a potential equivalent to a point-plate spark-gap of 5 inches; the focal-heart distance was 8 inches, and 1.5 ma. of current flowed through the tube.

[12] Twelve or more.

to induce a permanent alopecia corresponding to the field of irradiation; a third degree radiodermatitis occurred in but one animal. The skin of the animals was found more resistant to roentgen rays than that of human beings. A more detailed description of these experiments will be found in the section dealing with the respiratory tract (q.v.).

The outstanding result was a definite and marked inflammatory reaction of the pleura and lung corresponding to the area exposed to the rays and leading to chronic pulmonary sclerosis, with thickening of the alveolar walls, reduction in size or obliteration of the air spaces, increase in connective tissue around the bronchi and blood vessels, and marked thickening of the blood vessels in the affected area. In one rabbit the pericardium underwent serofibrinous inflammation, and in one dog the anterior wall of the right auricle of the heart was thickened and numerous petechial hemorrhages were noted in the pericardium. Davis seems to have looked on these cardiac changes as direct or primary effects of the rays.

Hallheimer and Schinz (1925) attempted to determine the influence of roentgen rays on the oxidases in the cardiac muscle, skeletal muscle, diaphragm, testis, and skin of guinea pigs. The technique of Gräff was used to determine the oxidases in the tissues, and special attention was given to the optimal hydrogen ion concentration. The animals used for *in vitro* experiments were killed by a blow on the head, and some of the organs were irradiated[13] in physiologic salt solution, some for one and some for two hours, while others were exposed to the rays without solution (dose approximately 600 per cent E.S.D., or 36000 R). Some of the guinea pigs were exposed through a diaphragm cone (small field), others were irradiated *in toto*. Parallel experiments were conducted *in vivo*. Sections of the control tissues were cut at the same time as the irradiated material; after exposure some of the sections were kept on ice, some at room temperature, some in physiologic salt solution, and some were kept dry. The sections were cut with a freezing microtome after the fresh organs were imbedded in 2 per cent agar cooled to 40°C., in which the organs were placed and rapidly frozen. The sections were placed either directly in the oxidase solution or in distilled water for five minutes at most, so that reaction of the unirradiated and irradiated material could be started at the same time and thus better compared. To ascertain the labile and stabile oxidases, a mixture of known pH was prepared according to the method of Gräff.[14] One cubic centimeter of a 10 per cent alcohol (90 per cent) standard solution of alpha-naphthol was added to 3 or 4 cubic centimeters of absolute alcohol and diluted with 95 cubic centimeters of distilled water. 0.6 gram of dimethyl-paraphenyl-endiamin-chlorhydrate was weighed and distilled in 500 cubic centimeters of distilled water. To regulate the pH (for enzyme studies by the method of Sorenson) secondary sodium phosphate, 11.9 grams of which was dissolved in warm distilled water and made up to 100 cubic centimeters with distilled water, was used. A definite quantity of the buffer solution was added to equal parts of the first two solutions, i.e. 20 cubic centimeters of buffer solution to 5 cubic centimeters of the mixture (2.5 c.c. of alpha-naphthol solution and 2.5 c.c. of dimethyl-paraphenyl-endiamin-chlorhydrate equals Nadi, according to Gräff). The result was a mixture of 0.1 per cent, with a pH of 8.1. The solution, which could be used after filtration, was poured in watch glasses and the sections placed in it for from five to thirty minutes.

A diminished reaction in the control sections, which had been subject to the action of distilled water for such a short time, could never be observed. The muscle fibers of the heart, of which only the myocardium was examined, always gave the same granular and diffuse reaction. Irradiated and unirradiated pieces of heart muscle did not show any constant difference. All the muscle fibers in the same section reacted with equal intensity as to granules and protoplasm. The reaction after six hours was the same.

[13] The rays were generated at a potential equivalent to a parallel, point-to-point spark-gap of 24 cm., and were not filtered. The current was 2.5 ma., and the focal-object distance was 23 cm.

[14] In Abderhalden's Handbuch d. biol. Arbeitsmethoden. Lfg. 78, 1922, Berlin & Wien, Urban & Schwarzenberg.

KRONTOWSKI (1925), exposed to roentgen rays[15] for 100 minutes, at a temperature of 37°C., eggs[16] containing four-day-old embryos, while other eggs were irradiated for the same length of time at a temperature of 25°C. Twenty-eight explant cultures were made from the irradiated embryos and twenty cultures from the controls. All the embryos irradiated at 37°C. and 25°C. died in a short time. However, cultures from the irradiated embryos in chicken plasma, with and without the addition of embryonal extract, grew well. Three such cultures were transferred and all three developed satisfactorily during the next eleven days, when the experiment was discontinued. One of these three subcultures was an explant from the heart of a chick embryo. At the time the culture was made the heart of this irradiated embryo was speckled with minute hemorrhages and did not beat. Nevertheless, uniform rhythmic contractions were perceptible in the culture after twenty-four hours; after forty-eight hours these contractions became weaker and less frequent, but after irrigating the culture and renewing the nutrient solution, the rhythmic pulsations improved and continued during the remainder of the experiment. Krontowski concluded, therefore, that exposure of the embryo to a lethal dose of roentgen rays does not prevent tissue cultures from such irradiated embryos from living and growing, even when the embryo was dying or actually dead when the cultures were made.

TSUZUKI (1926) exposed the entire body of rabbits[17] to roentgen rays of short wavelength.[18] The rabbits were irradiated in a wooden box at a uniform focal-skin distance of 40 cm. and given doses varying between 10 per cent and 160 per cent of the human erythema dose in from fifteen to 240 minutes. It was estimated that 80 per cent of the surface dose reached the kidneys. In one experiment twenty-nine rabbits received from 20 to 100 per cent of the human erythema dose at one sitting, and the effect was observed over a period of fifty-six days. All the internal organs were subjected to macroscopic and microscopic inspection. A single irradiation of over 40 per cent of the human erythema dose resulted in death sooner or later. More or less extensive pathologic disturbances were found in many organs including the lungs, liver, kidneys, and bone marrow, but the earliest and most pronounced effects were on the different elements of the lymphatic system and on the genital glands. No mention of cardiac abnormalities was made in connection with this series of experiments.

In a second series of experiments twenty-three rabbits received from 10 to 80 per cent of the human erythema dose in from fifteen to 120 minutes, and were killed at intervals of from fifteen minutes to ninety-six hours after irradiation. Again, more or less extensive alterations were found in many organs, much as in the first series. The only abnormality noted in the heart was not found until thirty-six hours after irradiation and consisted in fatty degeneration of the muscle cells. In a third series of experiments six rabbits were exposed to roentgen rays continuously until they died. Two succumbed after 180 minutes of irradiation (120 per cent of the human erythema dose); one after 200 minutes (130 per cent of the human erythema dose), and one after 220 minutes (150 per cent of the human erythema dose); the two remaining animals were irradiated for 240 minutes, one dying one hour, and the other two hours, afterward. Marked hyperemia of most of the organs, extensive destruction of lymphocytes in the spleen, mesenteric lymph nodes, intestinal lymph follicles, bone marrow, and thymus, degenerative changes in the testis, kidneys, salivary

[15] Coolidge tube operating at a potential equivalent to a spark-gap of 40 cm; focal-egg distance, 22 cm.; intensity of current, 2 ma.; unfiltered rays, the quality of which was 12 Wehnelt. The eggs were irradiated in a dish kept warm by means of a Sachse inductor.

[16] Incubated four days at a temperature of 37°C.

[17] Age, sex, and weight not stated.

[18] Generated in Coolidge "deep therapy" tubes excited by an oil-insulated, Neo-Intensiv Reform alternating current transformer, under the following conditions: Primary voltage, 220 volts at 50 cycles; secondary voltage, 170 peak kilovolts; secondary current, 2 ma.; filter, 0.5 mm. copper and 1.0 mm. aluminium; parallel spark-gap, 25 cm.; maximum secondary voltage measured by minimum wave-length, 139 kilovolts (0.09 to 0.30 Å—average about 0.14 Å); absorption coefficient for water, $\lambda = 0.164$; depth dose (10 cm. deep; focal-skin distance 23 cm.; field 6 × 8 cm.), 18 per cent; the human erythema dose required 50 min. at a focal-skin distance of 23 cm.

glands, and liver, and desquamation of the bronchial epithelium, edema, and simple or hemorrhagic exudation of the lungs were noted. Fatty degeneration of the muscle fibers was the only abnormality found in the heart.

Hartman, Bolliger, Doub, and Smith (1927) exposed to roentgen rays[19] the anterior thoracic wall of thirteen dogs and five sheep through a field 7 by 9 centimeters and 10 by 12 centimeters, respectively. The animals were kept in position by means of a specially constructed, adjustable holder. The electrocardiograph was connected in the usual manner, and sedatives or anesthetics were not employed. Three of the dogs, which had been irradiated for from 75 to 280 minutes, died within thirty days, apparently from causes unrelated to the irradiation. Five of the sheep, which had been exposed to the rays for from 120 to 280 minutes, also died within thirty days, apparently as a direct result of irradiation. These dogs and sheep ate well and most of them remained in a good state of nutrition, but some were abnormally quiet and tended to lie around in the cages. The remainder of the animals survived for three months or longer. In the animals surviving less than thirty days, the skin of the exposed territory usually exhibited depilation and often ulceration also. Passive hyperemia and edema of the thoracic tissues in the field of irradiation were found at necropsy; the skin was abnormally thick and tough. Passive hyperemia of the abdominal organs was constant. The lungs of the sheep, especially the lower lobes, were voluminous, and scattered patches of thickening were visible in the pleura, but effusion did not occur. On section the lower lobes were almost solid and contained a large quantity of thin, foamy fluid. The pericardial sac of all the sheep contained from 80 to 150 c.c. of fluid, but the pericardium throughout was smooth and glistening. The heart was distended from two to three times beyond the normal size, and this dilatation affected chiefly the right auricle and ventricle. Microscopic examination of sections from the wall of the right and left ventricles and interventricular septum disclosed swelling, a velvety appearance, indistinctness of the striations, and irregular staining of the fibers, hyperemia of the interfibrillar capillaries, occasional extravasations of blood, and moderate infiltration by round and wandering cells. Intense polymorphonuclear infiltration of the cardiac muscle was found in one of the sheep which had been irradiated for 240 minutes within thirty days. The branches of the auriculo-ventricular bundle, however, were comparatively well preserved and showed only thinning of the fibrils at the margins of the cells, and vacuolization, distortion, and shrivelling of the nuclei, but gave no evidence of hemorrhage.

Four dogs, which had been irradiated over the anterior thoracic wall for from 130 to 155 minutes in from three to five months, remained in good condition, but two developed late ulceration and cachexia. The cardiac abnormalities found at necropsy were of the same character as, but more marked than, in the animals that died within thirty days. The right auricle always gave evidence of a hemorrhagic process resembling that described by Davis; this sometimes extended through the auricular wall and sulcus terminalis at the base of the superior vena cava and around the pulmonary artery. Thrombosis of the tip of the auricular appendage was noted in some instances. The valves were always intact. The wall of the right ventricle averaged from 2 to 4 millimeters, and that of the left ventricle from 5 to 9 millimeters, in thickness. Areas of homogeneous, pink-staining, hyaline degeneration largely replaced the auricular muscle tissue, and such areas were surrounded by marked hemorrhagic infiltration. Some of the muscle fibers appeared as tubular structures filled with vacuoles, and suitable stains showed the fibers infiltrated with small and large fat globules. The walls of the blood vessels were thickened or actually obliterated. Serial sections through the sulcus terminalis, in three animals, revealed such extensive degeneration that the structure of the nodes could not be recognized. Hemorrhage and hyaline

[19] The rays were generated by a water-cooled tube operating at 200 kilovolts, filtered through 1 mm. of copper and 1 mm. of aluminium, at a focal-skin distance of 50 cm., with 30 ma. of current. Under these conditions an exposure of 15 minutes represented one human erythema dose.

degeneration were not found in the wall of the right and left ventricles or in the interventricular septum. Instead, atrophy of the muscle fibers, with indistinct striations, and granulation and vacuolization of the cytoplasm, were found. Many fibers were replaced by homogeneous, hyaline material. The interstitial tissue was abundant and finely granular or vacuolated, especially around the small blood vessels. The walls of the vessels were abnormally thick and their lumen narrow.

The entire anterior thoracic wall, including the region of the liver, of a second series of eight dogs was irradiated through a field 15 by 15 centimeters, but the dose given to each animal, the number of exposures, and the interval between the exposures were not specified. An effort was made to exclude the stomach and intestine from the path of the rays. More pronounced fibrosis of lungs and liver was found, but the cardiac alterations resembled those noted in the animals of the first series.

The right side of the thorax of three other animals was exposed to roentgen rays through a field 7 by 9 centimeters. Two of the animals apparently survived an unspecified dose of radiation, since only one, which had been irradiated for 190 minutes in four months, came to necropsy. This animal, weighing 25 kilograms, had remained fairly active and well nourished, but became cyanotic on exertion. The abnormalities noted included: hyperemia of the abdominal organs and kidneys; thickening of the pleura and focal pulmonary fibrosis; moderate hydropericardium, with a smooth membrane; a heart weight of 139 grams; roughening and grayish-red color of the lower half of the right ventricle and tip of the left ventricle; grayish-red color of the auricles, without thickening or hemorrhage; gray and reddish-brown mottling of the portion of the ventricular walls corresponding to the roughened area of the epicardium; softening of the interventricular septum; thickening and hyaline degeneration of the epicardium; hemorrhage, atrophy, and granular and vacuolar degeneration of the muscle fibers; and degeneration and atrophy of the muscle fibers of the right auricle, without hemorrhage.

In the five sheep, which died within a month from pulmonary edema and cardiac insufficiency, the electrocardiographic changes were limited to an inversion of the T waves in one or more leads, with an occasional, slight prolongation of the conduction time. The electrocardiographic tracings in the dogs were made without morphine or anesthesia. Inversion of the T waves in all three leads was found in almost every animal within the first or second month. Inversion limited to lead I, to leads I and II, and rarely to leads II and III, was found in a few instances. While no great importance was attached to such alteration, it was noted that, in dogs subjected to successive exposures to roentgen rays, marked inversion of the T wave often followed the first exposure, and the T wave flattened during the ensuing month, but deep inversion of the T wave again appeared after the second exposure. Abnormal T waves suggesting coronary obstruction were noted in two instances. Another early effect was a slight enlargement of the P waves in lead II, but the form and sign of the P waves were seldom altered. A moderate increase in voltage of the QRS complexes in leads II and III often was noted at this period. The conduction time was occasionally prolonged, but the P-R interval was seldom altered to any extent. Consistent increases in rate became apparent during the second month or later. Such simple sinus tachycardias later gave way to ectopic rhythms of from 300 to 345. The effect of vagus pressure, recorded on only one dog, represented a ventricular standstill, without preliminary slowing such as is usually seen in auricular flutter. The rapid rate was ascribed to paroxysmal tachycardia. Auricular flutter was recorded in four dogs, and in one animal the flutter continued for ten days. All the dogs in which auricular flutter and fibrillation occurred after irradiation presented, at necropsy, extensive hemorrhagic infiltration of the right auricle. Abnormal QRS complexes were found in only one animal, which had been irradiated exclusively through the right side of the chest.

Hartman, Bolliger, Doub, and Smith concluded that sufficient doses of roentgen rays may injure the heart, that roentgen irradiation provides a non-surgical experimental method of

inducing the myocardial lesions and electrocardiographic abnormalities described, and that auricular flutter and fibrillation also may be produced in this manner without the use of drugs or anesthetics.

SCHUBERT (1927), stimulated by the work of Krontowski, carried out similar investigations, using the exact explantation method described by the latter. Schubert was particularly interested in verifying Krontowski's observation that a lethal dose of roentgen rays applied to the chick embryo *in ovo* does not affect tissue cultures from the same animal and, more specifically, that on explantation immediately after irradiating the embryo in the egg no injurious effect can be detected. For culture purposes a medium consisting of one part of human plasma and one part of chicken embryo extract[20] was employed. After preliminary tests to determine the absolute lethal dose of roentgen rays for chick embryos *in vivo*, 10 skin erythema doses of unfiltered rays[21] were adopted and used throughout. Schubert found that exposure to filtered or unfiltered rays did not make an appreciable difference and that his results confirmed those obtained by Krontowski with a different technique. Cultures of cardiac, epithelial and other tissues, from embryos irradiated *in ovo* with a dose known to prevent further development of the embryo, grew at the same rate as control cultures. Pieces of heart explanted immediately after irradiation did not give cultural evidence of injury. From this it was inferred that injury to tissues from irradiation *in ovo* is gradual and results from the interaction or accumulation of many factors, and that when the tissue is removed from the organism such factors cease to act.

When tissue from the heart of a chick embryo irradiated *in ovo* was transferred to an unirradiated medium after varying intervals, the first signs of inhibited growth were noted in tissue explanted two hours after irradiation; tissue explanted three or more hours after irradiation always failed to grow. Death of such tissue was thought to result from processes within the organism released by exposure to the rays. Even one hour after irradiation, however, the heart had ceased to contract, and such contraction could not be stimulated by irradiation. The biologic processes involved were studied further by reversing the experimental steps in relation to irradiation. Instead of transferring irradiated cardiac tissue to unirradiated media, unirradiated cardiac tissue was now explanted into media irradiated *in ovo*. The growth of cardiac tissue in irradiated embryo extract was satisfactory when the explanted tissue was closely applied to the cover glass. To distinguish the specific effect of roentgen rays and the influence of other autolytic processes on the death of the embryo in the egg, it was necessary to explant heart tissue into embryo extract obtained from animals killed by some method other than irradiation. Lethal chilling was effected by placing the incubated egg in an ice mixture for one hour. Then the eggs were replaced in the incubator for a definite period, after which the extract was prepared. The growth of cardiac tissue explanted from animals chilled *in ovo* three hours previously was not inhibited. But growth was appreciably checked when the tissue was transferred to extract prepared from animals irradiated *in ovo* three hours previously. Tissue transferred to extract of embryo chilled twenty-four hours previously showed marked inhibition of growth. Tissue explanted from animals that, twenty-four hours previously, had received a lethal dose of roentgen rays did not grow in such extract.

Schubert concluded that the biologic effects produced in embryo extract by irradiation or by freezing differ in quantity but not in quality. This deduction was thought to be confirmed by the observation that the intensity of culture growth was inversely proportional to the degree of hemolysis in the extract. Both the irradiated and frozen embryos gave evidence of marked hemolysis. The irradiated and frozen extracts differed spectroscopically from the

[20] As described by Erdman.

[21] The rays were generated by a Coolidge tube electrically supplied by a Reiniger, Gebbert and Schall transformer operated at 60 kv., equivalent to a parallel spark-gap of 37.5 cm.; the intensity of current was 2 ma. and the focal-egg distance, 20 cm. Under such conditions, 1 erythema skin dose required exposure for 2.5 minutes.

control extracts only in that the former gave the characteristic absorption spectrum of oxyhemoglobin, while in the latter oxyhemoglobin was not recognized. Also, in extract from embryos irradiated or frozen *in ovo*, the hydrogen ion concentration tended to be acid, while the controls gave a neutral or faintly alkaline reaction. Control extracts irradiated *in vitro*, on the contrary, continued to give a faintly alkaline reaction.

Karczag, Von Farkas, and Györgyi (1927) tried to ascertain the behavior of cultures of the skin and spleen of frogs[22], and of the heart of chick embryos, exposed to roentgen rays in artificially combined, electropic vital stains; they also sought to determine whether vital stains induced in such cultures a biological or physico-chemical change. The preparations were irradiated[23] for from three to ten minutes, and the staining material was added after exposure. The results were not given in detail; only the main findings were stated. The epithelium and cultures of the spleen of the frog showed no change in the storage rate for stains and carbinol under roentgen irradiation. The elements which are not carbinolotropic under ordinary conditions did not present any variation in this respect under roentgen rays. The fibroblasts behaved in the same manner, but after deleterious doses of radiation did not take up stain or carbinol. Karczag, von Farkas, and Györgyi interpreted this absence of biologic action, even after strong doses of roentgen rays, as meaning that the colloido-chemical or physico-chemical disturbances caused by irradiation are within physiologic limits and are compensated for by the organism.

Stephens and Florey (1927), stimulated by the experiments of Swann, which appeared to show that "X-rays cause a gradual and regular fall of mean blood-pressure," undertook to determine if, under any conditions, exposure to roentgen rays induces the appearance of a depressor substance in the circulation. The entire body of an intact rabbit was irradiated[24] without anesthesia for seven hours, the exposure being interrupted for a few minutes from time to time. Blood was then collected from the ear vein and heparin used to prevent clotting; blood from a normal rabbit was collected as a control. From a third animal a blood-pressure tracing was taken from the carotid, after 5 c.c. of blood from the normal rabbit had been injected into the ear vein. The blood pressure fell momentarily 5 mm., but the pressure immediately returned to its former value; this slight change was ascribed to the act of injection, because a similar change followed the injection of normal saline. An identical effect was produced by injecting 5 c.c. of blood from the irradiated animal. Evidence of a depressor substance not having been obtained, it was thought that the fall in blood pressure noted by Swann might have been due to anesthesia. An animal anesthetized with urethane was, therefore, irradiated for three hours, and a heparinized sample of blood tested in the same way, but the blood pressure was not perceptibly influenced. After such prolonged irradiation the animals appeared to be in normal condition.

The death of a rabbit after irradiation for ten minutes, as described by Swann, pointed to some factor beside roentgen rays. In Swann's experiments the entirely unprotected animals had been placed at a distance of from ½ inch to 2 inches from the tube. Electrical leakage through the animal from the tube and high-tension leads was inevitable, especially with the animal lying on a copper table. To obviate this source of error, a metal box, with a window of aluminium foil 0.005 mm. thick immediately above the animal, was used as an electrical screen. In this electrical screen was placed an urethanized rabbit, and a record of its blood pressure was taken from the carotid artery. The rabbit was then irradiated continuously for one-half hour; instead of showing the expected fall, the blood pressure had risen to 10 mm. Further irradiation for one-half hour, without the electrical screen, was accompanied by a

[22] The number of animals was not given.

[23] The rays were generated by means of a radiotransformer operating at a potential of 170 kv., with 4 ma. of current, at a focal-skin distance of from 17.5 to 50 cm., and without filtration. The dose was not otherwise described.

[24] Rays generated by a gas tube operating at a potential equivalent to a spark-gap of 12 cm., with 2 ma. of current, at a focal-skin distance of 13 cm. Only a layer of cardboard 0.5 mm. thick intervened between the animal and the tube.

slight continuous fall in pressure. This was repeated six times with identical results. Moreover, it was impossible to cause a marked fall in blood pressure, even when the electrical screen was removed.

To test the effect of roentgen rays on respiration, a rabbit was anesthetized with urethane, then subjected to continuous irradiation[25] for one hour, partly with and partly without the electrical screen; during this time a respiratory tracing was made from a tracheal cannula. The irradiation had no demonstrable effect on respiration, and a repetition of the experiment also yielded a negative result.

The immediate effect of roentgen rays on the spleen and heart was then investigated. For the spleen a rectangular area of the previously depilated abdominal wall of young cats[26] was removed under ether and chloroform anesthesia. The incisions were arranged so that the interval between the margins of the cut skin and muscles was about 1 cm. after allowing for retraction. A celluloid plate[27] was then sutured to the muscle with close, interrupted, silk sutures. Complete hemostasis was essential. The celluloid overlapped the muscle by at least 1 cm. After suturing the plate to the muscle, the cut edge of the skin was sutured to the edge of the celluloid plate to avoid any "dead" space. The junction of skin and plate was sealed with small pieces of cotton-wool soaked in compound tincture of benzoin (B.P.) and, after drying, coated with collodion. The cat, with the exception of the head, was then covered with a thick layer of cotton wool and immobilized in plaster-of-Paris bandages to control the violent movements associated with recovery from the anesthetic; the plaster was removed after ten hours. The animal was irradiated on the third day, when it had recovered sufficiently to walk about the room. In a decerebrate cat a window over the heart also was inserted; during this operation the animal was kept alive by means of artificial respiration. Portions of the lung overlapping the heart were ligated and removed. The thoracic window was made air-tight; most of the air was removed by suction; the animal was allowed to resume normal breathing, and lived four and one-half hours with a very active heart. The animal was then exposed to roentgen rays for four hours, but no difference in the volume of the spleen could be detected, and the animal appeared to be perfectly well. When the cat was subsequently killed by chloroform, the spleen contracted to about two-thirds of its former volume. The decerebrate animal, with a transparent window over the heart, was irradiated continuously for one and three-quarter hours, but no difference in its action could be perceived. Stephens and Florey concluded that the positive results of irradiation reported by Swann were due to high-tension electrical discharges and not to roentgen rays, and that their own experiments failed to demonstrate any immediate effects of irradiation on cardiac function, blood pressure, respiration, or on the volume of the spleen.

Schubert (1927) undertook to ascertain the time, after irradiating chick embryos left in the egg at which inhibition of growth would appear and death of tissue follow, the presence of growth-inhibiting elements in the fluids bathing the cells, the physico-chemical nature of such alterations in cellular environment as might be found, and the influence of changes in the quality of radiation on the growth of the cultures. Tissue from the heart of chick embryos from nine to ten days old was used. After removal from the embryo, the heart was placed in Ringer's solution, cut into tiny pieces, and again washed in Ringer's solution. The pieces were then immediately distributed on cover glasses and a drop of culture medium was added to each piece; in this way the explants adhered well to the cover glass. The cover glasses were transferred to the concave slide, the entire ring of which was bordered with yellow vaseline, and the explant with the culture medium hung in the cavity. The cultures were now placed in the incubator. The culture medium consisted of equal parts of human plasma[28]

[25] Rays generated at a potential equivalent to a spark-gap of 11 cm., with a current of 1.5 ma., at a focal-skin distance of approximately 15 cm.

[26] Number and age of animals not given.

[27] Photographic film freed from gelatine and sterilized in mercuric chloride solution.

and extract of chick embryo.[29] The mixture of plasma and extract was prepared immediately before the medium was added to the cultures. In subsequent experiments only embryo extract was used as a medium. The cultures were inspected twice daily for three or four days; after this the cells degenerated rapidly unless the nutrient medium was changed. The composition of the culture medium was not uniform; sometimes it was obtained from irradiated, sometimes from frozen, embryos. Great care in the preparation of the medium was required to achieve approximately uniform results, but in spite of this, unexplainable daily variations occurred.

In order to obtain observable effects within four days, it was necessary to employ strong doses of roentgen rays—doses several times greater than those necessary to kill the embryo *in ovo*. The dose required to kill the embryo *in ovo* within twenty-four hours was first determined, and this proved to be about 5 E.S.D.[30] The eggs and cultures were, therefore, exposed to twice this dose, or 10 E.S.D.[31] of unfiltered roentgen rays for twenty-five minutes at incubator temperature.[32] The cover glass, with the preparation to be stained, was carefully raised from the slide, the culture medium removed with a fine glass pipette, and Orth's mixture pipetted on to replace the medium. This was left for one-half hour, after which the preparation was washed with distilled water and placed in 70 per cent alcohol. The preparation was then allowed to remain for twenty-four hours in stain composed of 30 c.c. of water and 30 drops of Delafield's hematoxylin. This was followed by washing with running water, differentiation in 1 per cent hydrochloric alcohol, fresh washing with running and then with distilled water, passage through alcohol of increasing strength into absolute alcohol and xylol, into pure xylol, and imbedding in oil of cedar.

Twelve hen eggs, with living embryos incubated nine days, were divided into four groups. After the nine day incubation period, the eggs of the first group were kept in the incubator to serve as controls. Three days later the eggs were opened to check the development of the embryos (now twelve days old). The eggs of the second and third groups were exposed to 10 E.S.D. of unfiltered roentgen rays on the ninth day of incubation and were returned to the incubator immediately afterward; when they were opened three days later, the dead embryos showed bloody imbibition and some were macerated. The embryos of the third group were removed from the eggs directly after irradiation, and heart cultures were placed in the plasma extract medium. Most of these cultures showed beginning growth after twelve hours of incubation; all showed growth after twenty-four hours, and growth continued for three or four days, when degeneration appeared and the cultures died during the next twenty-four hours. The unirradiated, control eggs of group four were opened and heart cultures made as in group three; some of these were kept as controls, while others were irradiated immediately after culture. No essential difference between the embryos or cultures of groups three and four was found.

In other experiments undertaken to test the effect of roentgen rays of different quality, the cultures, immediately after preparation, were exposed to 10 E.S.D. without filter, to 10 E.S.D. with 1 mm. of aluminium, to 10 E.S.D. with 2 mm. of aluminium, and to 10 E.S.D. with 3 mm. of aluminium. This did not have any perceptible influence on the growth of the cul-

[28] The blood was withdrawn from the vein with a vaselined cannula and syringe and immediately centrifuged in paraffined tubes on ice for three minutes. The supernatant plasma was removed with paraffined pipettes and placed in paraffined tubes on ice.

[29] The embryo extract was obtained by cutting embryos into small pieces, and the pap was centrifuged cold in paraffined vessels.

[30] Erythema skin doses.

[31] The rays were generated in Coolidge tubes by an Apex apparatus (Reiniger, Gebbert and Schall), at a potential of 120 kilovolts measured with a sphere-gap according to Holzknecht-Spiegler (point-plate spark-gap of 37.5 cm.; the current was 2 ma.; the half-value layer of the rays, according to Christen, was 2.5 cm.; the E.S.D., without filter, at a focal-object distance of 20 cm., required 2.5 minutes; with 1 mm. of aluminium, 6 minutes; with 3 mm. of aluminium, 9 minutes.

[32] Temperature maintained by means of an electric pad at 30°C. plus the heat from the glow-anticathode of the tube. The light from the tube was excluded by covering the cultures with black paper.

tures during the three days of observation. Schubert interpreted his findings as substantiating those reported by Krontowski.

The next step was to determine the time necessary for the effects of irradiation to manifest themselves in cardiac tissue from embryos irradiated *in vivo*. Chick embryos nine to twelve days old were exposed, while still in the egg, to the usual dose of roentgen rays and replaced in the incubator. The embryos were subsequently removed from the eggs at varying intervals, and cultures of cardiac tissue were planted in unirradiated medium consisting of equal parts of human plasma and extract of chick embryo. Cardiac tissue explanted four, six, and twenty-four hours after irradiation gave no evidence of growth, but some of the cultures made three hours after exposure of the embryo to the rays showed slight growth. Cultures made less than two hours after irradiation grew as well as the controls. After prolonged washing of the small pieces of cardiac tissue in Ringer's solution, irradiation had less effect on the growth of the cultures, or the interval between irradiation and explantation could be increased without greater inhibition of growth. This was assumed to mean that some of the products of irradiation were removed by the Ringer's solution. The time after irradiation at which tissue changes became apparent also varied with changes in the culture medium. When the medium consisted only of extract of embryo, injury and death of the cardiac tissue required a longer time. This was accounted for by the assumption that pure embryonal extract contains a larger quantity of growth-stimulating substances (hormones or enzymes). When cardiac tissue in culture medium was inspected microscopically from one-half to three hours after explantation, contraction was not observed; after five hours or longer the cultures had recovered from the mechanical injury incident to explantation, and distinct contraction could be seen in some of them. Such contraction could still be noted after the cultures had been replaced in the incubator for three or four days. Contraction could also be observed in cultures so injured by irradiation that growth had ceased twenty-four or forty-eight hours previously. When exposed to light, the contraction of the cardiac tissue was sometimes so great that the growth zone of fibroblasts slowly separated and displaced itself in the direction of the center of the explant. This was regarded as a mechanical effect of contraction. Correlation of the foregoing results was thought to indicate that the changes described were due largely to the secondary influence of products of decomposition induced by irradiation.

In order to study separately the tissue injury from products appearing in the tissue fluids as a result of exposure to the rays, Schubert reversed the experimental conditions by making cultures of unirradiated cardiac tissue in media irradiated *in ovo*. Eggs containing embryos from nine to twelve days old were exposed to the normal dose of roentgen rays, and after a certain period of incubation, the embryos were removed and used for the preparation of an extract, which was mixed with equal parts of human plasma. Into this medium pieces of cardiac tissue from other unirradiated embryos of the same age were explanted. A distinct inhibition of growth was never observed under these conditions, and this was considered due to the fact that fresh human plasma partly compensated for the injurious action of irradiation on the extract. Control cultures in pure embryonal extract grew as well as in combined extract-plasma medium. To remove the objection that the products appearing in the tissue juices might result from the death of the embryos through causes other than irradiation, normal cardiac tissue from an animal killed by exposure to cold was explanted into embryonal extract prepared after irradiation, freezing, and incubation. The cultures in extract prepared from embryos irradiated four hours before showed slight inhibition of growth, but no such inhibition occurred in tissue cultured in embryo extract frozen four hours previously. Slight retardation of growth also was noted in cultures explanted in embryo extract prepared three hours after irradiation. When the time between irradiation of the extract and explantation was shortened, no difference between the experimental and the control cultures in fresh extract could be perceived. By gradually increasing the time between irradiation and freezing and the preparation of the extract, it was found that growth did not occur when the tissue

was explanted in embryo extract which had been irradiated *in ovo* twenty-four hours previously, while the growth in extract frozen as long before was distinctly inhibited. Thus it was shown that the growth of cultures was deleteriously influenced by substances in the tissue juices arising from ordinary autolytic processes, but that such influence was still greater when the tissue was cultured in irradiated extract. Fresh extract of embryo was also irradiated *in vitro*, used for cultures twenty-four hours later, and then kept in the ice box, but this did not have any apparent effect on the growth of the cultures.

When removed from the eggs the irradiated embryos showed marked extravasation of blood around the periphery, and the heart was white and devoid of blood. The frozen animals, on the contrary, were pale, and the blood had accumulated at the center. When centrifuged, the extract of irradiated and frozen embryos presented a bloody discoloration; the reddish color of the extract of irradiated embryos was more pronounced than that of frozen animals; this was attributed to hemolysis. Moreover, the greater the hemolysis the more deficient the growth of the cultures. To elucidate this phase of the problem, the embryo extracts were examined spectroscopically, and both the frozen and irradiated extracts exhibited the absorption spectrum characteristic of oxyhemoglobin. By adding ammonium sulfide the oxyhemoglobin was carried over into reduced hemoglobin. Methemoglobin was never found, and Schubert surmised that this may have been due to the relatively small dose of rays used to induce hemolysis or that the reactions *in vivo* and *in vitro* differ. The hydrogen ion concentration of the extracts also was tested by the electrometric, or gas-chain, method, with pear-shaped electrode vessels covered with 1.0 or 1.5 c.c. of the fluid to be tested. The extract was diluted 1 : 1 or 1 : 2 with 0.9 per cent of physiologic salt solution free from CO_2 and perfused in the electrode vessel with pure hydrogen gas for at least ten minutes. Both irradiation and freezing of the embryos *in vivo* caused the hydrogen ion concentration to be displaced toward the acid side.

The influence of so-called "grenz," or low-voltage, roentgen rays (Bucky) on the growth of tissue cultures was investigated. To prevent the rays from being absorbed by the cover glass, a metal plate with many perforations was placed 10 centimeters above the upper edge of a glass vessel 13 cm. high and 12 cm. in diameter, where it was suspended by a metallic connection. The glass cover of the vessel had a central opening 4 cm. in diameter, which could be closed by a Petri dish, and the entire device was sterilized in the autoclave. The cultures on the cover glasses were placed on the metal plate and the space under the plate was filled with water at 37°C. to keep the cultures warm and moist. The cover was closed and the cultures were irradiated[33] through the central opening. Immediately afterward, the cultures were placed on concave slides and ringed with vaseline. The control cultures grew normally. When the cultures exposed to 3 E.S.D. in 30 minutes failed to grow, the dose was gradually reduced, but exposure to even 1 E.S.D. was generally sufficient to prevent growth. A pronounced odor of ozone or nitrous gases was perceptible in the glass vessel during irradiation. By placing, 4 cm. below the opening in the glass cover, a metal plate which allowed the gases to pass freely on the side of the cultures, and by exposing these to 1 E.S.D., Schubert again found almost complete inhibition of growth and felt obliged to attribute this effect to the action of the noxious gases. To test this further, cultures were irradiated[34] in an atmosphere of carbonic acid gas, which was allowed to flow into the vessel from below throughout the period of irradiation. Control cultures were likewise exposed. Carbonic acid gas was found to inhibit growth, but irradiation increased the retarding effect. It was therefore concluded that so-called "grenz," or low-voltage, roentgen rays definitely inhibit the growth of tissue cultures; that the noxious gases generated by the apparatus exert a still greater influence on growth; and

[33] The rays were generated by a Bucky tube (F. Müller) operated by a Koch and Sterzel generator at an effective potential of 10 kilovolts, with a current of 10 ma. Under these conditions, irradiation for 10 minutes, at a focal-skin distance of 10 cm., gave a slight erythema after 3 or 4 days.

[34] 1.5 E.S.D. in 15 minutes.

that roentgen rays generated at such low voltage inhibit growth more than rays generated at higher voltage. Schubert interpreted the results of his experiments as indicating that the primary effect of irradiation was a modification in the permeability of the cells, and that products of decomposition altered the medium and secondarily influenced other cells.

HABERLANDT and SANDERA (1927) excised pieces of the sinus-auricle and of the base of the ventricle from two large *Esculenta*, freed them from blood, placed them in Ringer's solution, and then exposed them to 20 Holzknecht units of roentgen rays[35] for thirty minutes. Thirty similar preparations were irradiated in the same manner. The cardiac substance continued to beat in spite of such strong irradiation, and Haberlandt and Sandera deduced that the substance which maintains the cardiac impulse had not been influenced. In many of the preparations, on the contrary, they found that irradiation either set the tissue beating or was followed by an acceleration of the beat, and this increase in the pulse rate was sometimes too great to be caused by the slight warming of the preparation by heat from the tube. Moreover, the pulse rate attained its maximum in from five to ten minutes and then remained constant or decreased in spite of continued irradiation. It was also found that, in cases in which the pulse rate did not increase on exposure to the rays, warmth alone had no effect. Exposure to roentgen rays either set the tissue beating or induced regular contraction in seventeen preparations from the base of the ventricle, which had been quiescent before irradiation or beat only occasionally.

An inhibitory action on the muscle, whereby the pulse of the sinus-auricular pieces became constantly weaker and finally often stopped, also was observed during irradiation. This inhibitory action was transient and disappeared in from five to fifteen minutes after irradiation. Experiments with atropin apparently showed that it was not due to vagus action. From this it was deduced that roentgen rays had not destroyed the cardiac hormone and that the initial acceleration of the heart beat indicated a promoting influence of radiation on the formation of cardiac hormone and not a direct effect on the muscle fibers. These findings appeared to agree with those of Zwaardemaker and Feenstra, who found that the cathode rays had the property of initiating contraction, but also induced transient inhibition of the cardiac impulse in the heart of cold-blooded animals. A similar reaction was obtained in the excised heart of seventeen frogs, the cardiac region of each of which had been exposed to the same dose of roentgen rays or to doses twice as large from one to eight days previously. Aside from the heart, the behavior of the animals was quite normal. The same result was obtained on the excised whole heart of ten other frogs. On the contrary, watery solutions of cardiac hormone subjected to similar doses of roentgen rays generally lost their effectiveness. The effect of similar doses of roentgen rays on the heart of sixteen other frogs, exposed *in situ* under ether anesthesia, was to increase the rate and amplitude of cardiac contraction, but no evidence of transient inhibition could be obtained under these conditions. Haberlandt and Sandera concluded that the radiosensitiveness of the heart is very slight, and that the organ can tolerate enormous doses of roentgen rays without apparent injury.

WARTHIN and POHLE (1927) set out to determine the pathologic changes in the heart induced by roentgen irradiation of the cardiac region of thirty-two rats and twenty-five rabbits; five other rats and five rabbits were used as controls. Each animal was tied to a board, in supine position, with legs and body extended; the cardiac region was carefully localized by palpation and such localization was verified at necropsy. A precordial (anterior thoracic) field, 1.5. cm. square in the case of the rat and 2.0 by 2.5 cm. in the case of the rabbit, admitted sufficient radiation[36] to cover the entire cardiac area. Fields of this size were cut in sheets of lead 6 mm. thick, which shielded the remainder of the body from the rays.

[35] The unfiltered rays were generated by a Müller tube, at a potential of 44 kilovolts, with 4 ma. of current, at a focal-object distance of 30 cm. The shortest wave-length was $\mu = 0.28$ Å.

[36] The rays were generated by a Coolidge water-cooled tube operated in connection with a transformer with mechanical rectifier, at a potential of 200 kilovolts measured by means of a sphere-gap; 25 milliamperes of current passed through the tube; the rays were filtered through 0.5 mm. of copper and 1.0 mm. of aluminium, and the focal-skin distance was 40 cm. The

None of the animals died during or immediately after irradiation, or later, from causes traceable to such exposure. All the animals were killed by ether after varying intervals, and the thoracic organs were carefully removed so as to avoid mechanical injury to the heart, which was still beating when placed in 10 per cent solution of formaldehyde. Macroscopic changes were not observed in the irradiated heart of any of the rats or rabbits. After thorough fixation, the organ was hardened and dehydrated in graded alcohols, passed through xylene, and embedded in paraffin. In every case the entire heart of each rat was cut transversely into three blocks, and that of each rabbit into four blocks. After having been embedded in paraffin, each block was cut into serial sections; in the case of the rats all the sections were stained with hemalum and eosin, but in the case of the rabbits every tenth section was stained; all the sections were mounted in balsam in the usual way. To bring out fatty changes sections of myocardium were stained with Sudan III.

The cardiac region of four rats received at the cutaneous surface 100 per cent of a human erythema dose at one time, and the animals were killed the next day; the heart of one animal was normal. Sections of myocardium from another rat showed only diffuse Zenker necrosis, while sections from the two remaining animals presented, in one case, diffuse Zenker necrosis and slight lipoidosis, and in the other, diffuse Zenker necrosis, slight lipoidosis and areas of spontaneous myocarditis. The cardiac region of two other rats received 100 per cent of a human erythema dose, and the animals were killed two days later. In one the heart showed slight diffuse lipoidosis, marked hyaline change in the muscle fibers, and pycnosis of some of the nuclei; in the other, diffuse hyaline change of muscle fibers, and a pycnotic and granular appearance of some of the nuclei. The cardiac region of two other rats was exposed to 100 per cent of a human erythema dose, and the animals were killed seven days later. Only slight hyaline degeneration of the myocardium was found. The cardiac region of one rat was exposed to 100 per cent of a human erythema dose, and the animal was killed eleven days later. The vessels of the heart were dilated and gorged with blood (passive congestion). Degenerative changes in the heart or vessels were not observed. The precordium of another rat was exposed to 10 per cent of a human erythema dose; when the animal was killed, eleven days later, the coronary vessels were congested, but degenerative changes were not found.

The precordium of three rats was exposed to 100 per cent of a human erythema dose, and the animals were killed thirty-five days later. The heart was entirely normal. The precordium of three rats was exposed to 100 per cent of a human erythema dose, and the animals were killed forty-five days later. The heart of one rat presented marked and diffuse Zenker necrosis; that of a second rat showed slight diffuse Zenker necrosis, and that of the third rat showed marked Zenker necrosis. The precordium of eight rats was exposed to 100 per cent of a human erythema dose, and the animals were killed after an interval of sixty days. The myocardium of four rats was quite normal; that of two rats showed only slight hyaline change. In one rat slight lipoidosis of the papillary muscle of the left ventricle, and in another rat slight lipoidosis of the inner layer of muscle of the left ventricle, were the only abnormalities noted. Slight, diffuse hyaline degeneration was also observed in the myocardium of one of two control rats; the myocardium of the other unirradiated rat was normal.

The precordium of three rats received 200 per cent of a human erythema dose; two were killed the next day, while the third was allowed to live forty-five days. The myocardium of two rats (one killed one day, and one killed forty-five days, after irradiation) showed only slight diffuse Zenker necrosis; the myocardium of the remaining animal showed well-marked Zenker necrosis, and that of a control (unirradiated) rat presented evidence of early, diffuse Zenker necrosis. The precordium of two rats was exposed to 300 per cent of a human ery-

effective wave-length, determined by the method of Duane, was 0.16 Å. Under these conditions, the human erythema dose required nine minutes' exposure, and this was regarded as equivalent to approximately 1100 roentgens (American standard), as measured with an ionization chamber in air. It was assumed that about 80 per cent of the surface dose reached the heart muscle. In two rats exposed to unfiltered rays generated at a potential of 130 kilovolts, with 5 ma. of current, and at a focal-skin distance of 30 cm., the erythema dose required two minutes' exposure, or 370 r (in air).

thema dose, and both rats were killed the next day. The heart of one rat showed marked Zenker necrosis and early interstitial myocarditis; that of the other rat presented marked diffuse Zenker necrosis, inflammatory reaction in atrophic peribronchial fat tissue, acute purulent bronchitis, and atrophy of the bronchial lymphoid tissue. Another rat, the precordium of which received 400 per cent of a human erythema dose, was killed the next day; the myocardium showed marked, diffuse Zenker necrosis and slight lipoidosis of the subendocardial muscle. Marked Zenker necrosis, and areas of interstitial inflammation, especially in the auricles, were observed in the heart of one rat, the precordium of which had been exposed to 500 per cent of a human erythema dose, and which was killed the next day. In one rat, the precordium of which was exposed to 1000 per cent of a human erythema dose, and which was killed the next day, only slight, diffuse Zenker necrosis was found.

The precordium of four rabbits was exposed to 100 per cent of a human erythema dose, and the animals were killed the following day. The heart of one presented cloudy swelling and slight fatty, degenerative infiltration; the heart of a second rabbit presented Zenker necrosis and marked fatty degenerative infiltration; the myocardium of the two remaining rabbits showed diffuse fatty degenerative infiltration. The heart of an unirradiated, control rabbit displayed early Zenker necrosis and moderate fatty degeneration. The precordium of two rabbits received 100 per cent of a human erythema dose, and the animals were killed seven days later. The heart of one exhibited marked, diffuse lipoidosis and very slight hyaline degeneration; in the myocardium of the other were found slight lipoidosis involving chiefly the papillary muscles, marked hyaline degeneration, and pycnosis of the vascular endothelium.

The cardiac region of one rabbit received 100 per cent of a human erythema dose, and the animal died nine days later. The microscopic findings included atrophy of the heart muscle, fatty degeneration of the papillary muscles, and slight, diffuse hyaline degeneration. The cardiac region of one rabbit received 100 per cent of a human erythema dose, and the animal died nine days later. The microscopic findings included atrophy of the heart muscle, fatty degeneration of the papillary muscles, and slight, diffuse hyaline degeneration. The precordium of two rabbits received 100 per cent of a human erythema dose, and the animals were killed ten days later. Diffuse fatty degeneration of the myocardium of the left or of both ventricles, and slight granular changes in the nucleus of the muscle cells, were noted. Similar changes were observed in the myocardium of an unirradiated, control rabbit.

The precordium of three rabbits was exposed to 100 per cent of a human erythema dose, and the animals were killed fifteen days later. Well marked or moderate fatty degeneration of the inner layer only, or of both the inner and outer layers of the myocardium of the left or of both ventricles, was found in all three rabbits, and in addition the heart of one animal showed early hyaline change in scattered muscle fibers. The heart of an unirradiated, control rabbit showed slight changes of the same character. The precordium of three rabbits received 100 per cent of a human erythema dose, and the animals were killed thirty days later. The heart of one presented only slight hyaline change in the muscle; the heart of another showed well marked fatty degeneration and slight hyaline change of some of the muscle fibers; the heart of a third showed diffuse fatty degenerative infiltration, most marked in the inner muscle layer and papillary muscles of the left ventricle.

The precordium of three rabbits received 100 per cent of a human erythema dose, and the animals were killed forty-five days later. In all three rabbits, as well as in an unirradiated, control animal, the myocardium showed slight fatty degeneration and early or moderate Zenker necrosis. In the heart of four rabbits, the precordium of which had been exposed to 100 per cent of a human erythema dose, and which were killed sixty days later, marked fatty degenerative infiltration of the inner layer of the myocardium, and sometimes of the subepicardial layers, was noted. The same changes were found in the heart of an unirradiated, control rabbit. The precordium of two rabbits was exposed to 200 per cent of a human erythema dose; one was killed one day, and one forty-five days, later. The myocardium of the first animal showed fatty degenerative infiltration, especially marked in the inner layer; the myocardium of the second animal presented only slight, diffuse Zenker necrosis.

In commenting on their results, Warthin and Pohle explained that the Zenker necrosis may have represented in part a purely agonal condition increased by fixation of the beating heart in formaldehyde solution, the resulting muscular contraction giving the microscopic appearance of early and diffuse Zenker necrosis. They thought the lipoidosis probably represented a nutritional condition of the animal, doubted its pathologic significance, and did not consider this as directly related to irradiation. They admitted that both the Zenker necrosis and lipoidosis are "commonly associated with infections, anemia, and altered nutritive states." In only one rabbit could they regard the unusual degree of Zenker necrosis as an effect of the rays; in this instance 200 per cent of a human erythema dose had been given. In two rats, each of which had received 100 per cent of a human erythema dose and which had been killed two days after irradiation, the changes in the myocardium appeared sufficient to be considered as effects of irradiation. Warthin and Pohle concluded that a single exposure of the precordium to one human erythema dose of roentgen rays of the quality specified does not produce definite and irreparable injury to the heart of adult rats and rabbits.

Domagk (1928), without describing his experiments, stated that in rabbits, the entire body of which had been exposed to roentgen rays, he had often observed extensive changes in the heart muscle in the form of extensive fatty degeneration, loss of transverse striations, vacuolar degeneration, and focal necrosis. When the animals survived irradiation for a considerable time, interstitial proliferation of fibroblasts was noted.

Heim (1928) chose to study the action of roentgen rays on the germ cells and the embryo of the chicken, because previous experiments had led him to open more than 400 incubated eggs and he was familiar with the morphology of embryonal development. The object of this investigation was to determine the biologic action of roentgen energy on the fertilized egg irradiated before incubation, during the stage of the segmentation nucleus, and during the various stages of incubation, to follow the development of the embryo after irradiating the ovary of the hen, and to observe tissue explants of irradiated embryos in respect of growth and cellular function as compared with normal cultures. To avoid hereditary variations, only eggs from purebred white leghorns were selected. The hens and cocks, the living conditions, and the days of laying were thus accurately known. Only eggs kept at a cool temperature for less than ten days were used. The eggs were never irradiated[37] until twenty-four hours after being transported, to allow the effect of shaking to subside. The eggs were incubated in an electric incubator at 39° C., were ventilated twice daily, and were turned on their long axis at the same time. A pan of water provided the necessary moisture. The eggs were opened after about eight days, because it is well known that incubation for a longer time in an apparatus not providing adequate ventilation causes a larger number of embryos to perish.

In the initial experiment six eggs, three of which were fertilized, were exposed at the same time to 500 r of roentgen rays immediately before incubation. Four other eggs, three of which were fertile, were not irradiated, but were incubated with the others to serve as controls. All the eggs were opened on the ninth day of incubation. Though alive, the irradiated embryos displayed general inhibition of growth. Their length from coccyx to vertex was from 2.1 to 2.4 cm., while the controls measured 3 cm. One of the irradiated embryos exhibited bilateral microphthalmos, and another showed unilateral microphthalmos, and deformity of the brain. In a second experiment four eggs were exposed to 500 r of roentgen rays. The fertilization ratio of the irradiated and the control eggs was 4:4, and when they were opened, eight days and twenty-three hours after irradiation, inhibition of growth, with an average length of only 2.75 cm. as compared with the 3.2 cm. of the control animals, was found. One embryo measuring 2.7 cm. in length was hemorrhagic, and its heart had ceased to beat; its thoracic and abdominal organs lay external to the body fissure; the beak was

[37] The roentgen rays were always generated by a Stabilivolt apparatus operating at a potential of 200 kilovolts (170 effective resistance), a.e.g. tube, filtered through 0.8 mm. of copper and 1 mm. of aluminium, at a focal-egg distance of 30 cm.; and with 4 ma. of current. The e.s.d. equalling 500 r required 19 minutes.

blunt, the upper palpebral fold ill-developed, the margin of the pupil irregularly rounded, the periphery of the iris spotted and deficient in pigment, and the right pupil excentric and displaced caudalward. A second embryo presented a hemorrhage between the parietal halves of the brain. In a third experiment five eggs were exposed to 500 R of roentgen rays. Their fertilization ratio was 5:3, while that of the controls was 5:5. The embryo was absent from two of the irradiated eggs; two other embryos measuring 2.2 and 2.3 cm., in contrast to the 2.8 cm. of the controls, were living, but presented general inhibition of growth. A third measuring 1.8 cm. presented a hammer-shaped head, absence of eyes and beak, and an actively pulsating heart, with the large vascular trunks outside the thoracic cavity. Five other eggs were exposed to 250 R. All the embryos were living and showed inhibition of development, but to a less degree than in the preceding experiments. Their average length was 2.6 cm. Five eggs received a dose of 500 R, and, when opened eight days later, only two embryos were found; one measuring 0.35 cm. had apparently died early; the second was underdeveloped and measured 2.1 cm. Five other eggs received a dose of 250 R and were opened eight days later. Two undeveloped embryos, measuring 2.5 and 1.8 cm., respectively, were found, and one was distinctly ill-formed, with complete asymmetry of the body, hemorrhagic inhibition of one-half of the body, left anophthalmos, atrophy of the right eyeball, and asymmetric development of the brain.

In the second series of experiments the eggs were exposed to 100 R of roentgen rays on each of five successive days, and were kept cool between the irradiations. Their incubation began immediately after the last exposure and continued for nine days. The fertilization ratio of the irradiated eggs was 5:1, of the controls, 3:2, and only one was fertilized. This embryo measured 2.5 cm., and exhibited general inhibition of growth, such as absence of feather papillae. The toes, however, were well differentiated, the eyes normal, and the thoracic fissure almost closed. The controls measured 3.2 and 3.4 cm., respectively. The fertilization ratio of a second group irradiated similarly was 6:3, while that of the controls was 4:4. The average length of the control eggs after nine days' incubation was 3.6 cm., while the average for the irradiated eggs was only 2.5 cm., and the developmental deficiencies included inferior pigmentation of the iris and absence of feather papillae.

In the two next series of experiments the incubation was started eight days after irradiation, the eggs being kept cool during the interval. One group of five eggs, receiving 500 R of roentgen rays, showed a fertilization ratio of 5:2, and were opened after incubation for eight days and twenty hours. The first embryo had died early. The second measured 1.8 cm., and its heart did not beat; it also showed flipper-like, stumpy limbs, absence of feather papillae and beak, deficient and spotty pigmentation of the retina, general inhibition of development and died after some days. Five other eggs were exposed to 500 R, incubated immediately after exposure, and opened eight days and eighteen hours later. The first embryo, which was living and measured 3 cm., exhibited a wedge-shaped fissure in the upper portion of the iris of the left eye, and general retardation of growth. The second embryo, also measuring 3 cm., was dead. The trunk and head showed hemorrhagic discoloration, the wings were stumpy, the toes rudimentary, and the retina was spotted and deficient in pigment. The third embryo, measuring 2.3 cm., was dead and presented the same defects. The fourth embryo, measuring only 1.5 cm., showed bilateral microphthalmos, and its heart did not beat. The length of the control embryos averaged 2.85 cm. Ten other eggs, arranged on a surface approximately 25 cm. in diameter with three eggs in the center and surrounded by seven others, were exposed at the same time to 500 R of roentgen rays, incubated for eight days and three hours, and opened. The living, irradiated embryos showed only retardation of growth, but there was a distinct difference between those lying in the region of the central cone of rays and those on the outside of the circle. The average length of the former was 1.95 cm., while that of the latter was 2.2 cm. The centrally placed embryos were more delicate in structure and bright in color, and their retina contained less pigment. The thoracic fissure of all irradiated animals

was still open, while that of the controls was almost always closed. Heim deduced that the retardation of growth, the deformities, and the abnormal frequency of death among the embryos were a direct result of irradiation. Irradiation during the early stage of development caused the greatest retardation of growth, number of deaths, and occasional deformities, such as microphthalmos. Irradiation during the second third of incubation had less influence on growth, while no such influence was found in embryos irradiated during the last week of incubation.

Heim also tested the effect of irradiating the ovary on the subsequent development of the embryo. For this purpose the abdomen of a white leghorn hen one year old and laying well was exposed to one-half erythema skin dose (human) of roentgen rays[38] in six minutes. No eggs were laid during the next fourteen days, but after this the hen resumed ovulation at her previous normal rate, and the embryos were normal. Seven weeks after the first irradiation, one erythema skin dose (human) was given in the same manner in twelve minutes. Two eggs were laid during the next two days, but none were laid during the ensuing thirty days. The embryos in the two eggs, which were opened after incubating for six days and twenty-one hours, were dead; one measured only 0.2 mm., the other 1.1 cm. The left upper half of the second embryo was hemorrhagic; the edges exhibited unequal microphthalmos, and an excentric, protuberant, lenticular *anlage;* the head was small, rounded and asymmetric, and a hemorrhagic protrusion appeared on the vertex. In this instance death, inhibition of growth, and deformities were regarded as evidence of injury to the embryo itself. When, thirty days after the second irradiation, the hen resumed ovulation, the first egg had a thin shell, but the eggs laid subsequently were normal in appearance and number, and the embryos were normal. In all, 53 eggs from this hen, which had been irradiated twice, were incubated and examined in the course of five months. The same retardation of growth was noted as in irradiated eggs from non-irradiated hens, but the incidence of death and deformity was always less. No evidence of injury to the germ plasm was found. Aside from the transient cessation of laying, the hen remained in good health, behaved normally, and her laying power was in nowise affected.

Further experiments were undertaken to test the effect of irradiation on the developmental morphology of embryonal generations after roentgenization of the eggs, and the behavior of cell generations from irradiated embryos. Special attention was given to (1) the growth of explanted tissue embryos from eggs irradiated before or during incubation; (2) the functional reaction of the cells of such cultures to vital stains; and (3) the reaction to radium or roentgen rays of cultures growing *in vitro*, in comparison with explants from normal embryos. Pieces of the heart of chicken embryos from eggs exposed to 500 R of roentgen radiation before or during incubation were planted, according to Harrison's cover-glass method, in a mixture of chicken plasma and embryonal extract 1:1, and their growth was compared with normal cultures. Differences in storage behavior as an expression of altered cellular formation were also investigated by adding, after some days of growth, a drop of 1:1000 neutral red solution. At first the explants from irradiated embryos grew as well as the control cultures, but a tendency to premature degeneration and increase in mitosis subsequently became apparent. The results of many such experiments were so inconstant that no conclusion could be drawn.

Zwaardemaker and Feenstra (1928), claiming to have established that the heart of the frog, the rhythmic pulsation of which has been arrested by perfusion with Ringer's solution free from potassium, can be made to beat again regularly by perfusion with Ringer's solution containing a small quantity of radium emanation (dose of the order of $3.6.\ 10^{-4}$ ergs per hour), undertook to test the comparative effect of roentgen rays. Cathode rays[39] were

[38] Rays generated at a potential of 200 kilovolts, filtered through 0.5 mm. of zinc and 1 mm. of aluminium, at a focal-skin distance of 30 cm.

[39] The Crookes tube was operated at a potential of from 1700 to 2000 volts. With an aluminium window 8μ thick the vacuum was 17μ. On the average, the energy of the tubes was 0.25 ma-hr. with 3 ma. in the secondary circuit.

used in thirty-two experiments, in 76 per cent of which a sudden resumption of cardiac activity occurred during irradiation.[40] After the irradiation was discontinued, the heart again stopped beating, but in one-third of the cases rhythmic pulsation was resumed spontaneously and lasted several hours. The average time between the beginning of irradiation and the first systole was slightly less than one hour, and the first systole was followed by regular, rhythmic contraction for one and two-thirds hours, and by irregular contraction for seven hours, on the average. The heart was placed directly in front of the aluminium window and was thus exposed to the heat generated by the tube, but other experiments with radiating heat had never been followed by functional recovery of an organ abundantly perfused with potassium-free Ringer's solution.

Other experiments with an aluminium window and a tube energy of 0.22 milliampere-hours gave negative results, because "according to Kaye, the limits of the passage of cathode rays through aluminium had been reached." Seven experiments with an aluminium window 32μ thick had only a slight, apparent influence, which was thought to be due to the aluminium window having been made porous by the impact of the rays. Twenty-eight experiments[41] with double the energy[42] and an aluminium window 48μ thick gave a positive result in 80 per cent of the tests, and the character of the pulsations was the same as with the cathode rays, except that the post-irradiation effect was more pronounced and continued for twenty hours, on the average. Also, the functional recovery of the heart required approximately two hours. When the heart was exposed to the same radiation filtered through 80μ of aluminium, the immediate effect disappeared and only the late effect persisted; this was ascribed to difference in dosage. Many more experiments were made with very soft roentgen rays generated at a potential of from 4,000 to 11,000 volts, but positive results were obtained in only 30 per cent of the tests. The possible influence of heat could not be excluded. Zwaardemaker and Feenstra explained the foregoing results by assuming that irradiation activated the automatinogen in the arrested heart to automatin, and the perfused organ began to pulsate. The pulsations soon exhausted the automatin, and contraction again ceased, to be resumed at a slower rhythm when sufficient automatin had accumulated.

Warthin and Pohle (1929), having found in a previous series of experiments that a single exposure of the precordium to roentgen rays corresponding to a human erythema dose does not induce direct injury to the heart muscle of adult rats and rabbits, proceeded to investigate the effect of a series of exposures on the heart of thirty-seven rats and sixteen rabbits; ten other rats and five rabbits were left unirradiated to serve as controls. The thirty-seven irradiated rats were divided into three groups of nine each and one group of ten, and the sixteen irradiated rabbits were divided into one group of nine and one of seven. The precordium of each animal[43] was exposed, in the same manner as in their previous experiments, to an initial dose of 600 r and to two subsequent doses of 300 r at intervals of one month. Some of the rats[44] and rabbits[45] were exposed to rays of short wave-length,[46] while others were exposed to rays of longer wave-length.[47] The animals were killed from eight to thirty-two days after the last irradiation, and the heart was promptly removed and prepared for microscopic examination.[48]

[40] The period of irradiation averaged four and one-half minutes, distributed over a lapse of one and one-quarter hours. The method of irradiation was not described.

[41] The total duration of discontinuous irradiation was about ten minutes within one hour, on the average.

[42] The amount of tube energy was estimated as 0.5 ma-hr.

[43] In each animal the position of the heart was accurately determined by preliminary roentgenography.

[44] Presumably two of the four groups.

[45] Presumably one group.

[46] Rays generated at 200 kilovolts, filtered through 0.5 mm. of copper and 1 mm. of aluminium; intensity of current, 25 ma.; focal-skin distance, 40 cm.; time of exposure, 9 min.; effective wave-length in copper, 0.16 Ångström; human skin tolerance dose, measured with a Wulf ionization chamber in air, 600 r. Absolute standard obtained by means of an open-air ionization chamber in connection with a sensitive galvanometer, as suggested by Duane and Lorenz.

[47] Rays generated at 130 kilovolts, filtered through 4 mm. of aluminium; intensity of current, 5 ma.; focal-skin distance, 24 cm.; time of exposure, 6 min.; effective wave-length in copper, 0.23 Å; human skin tolerance dose, 300 r.

[48] The method of preparation was the same as in the preceding experiments.

All the irradiated rats and rabbits showed more severe degrees of Zenker's hyaline degeneration, necrosis and fatty degenerative infiltration than had been found in the previous experiments. Moreover, many animals presented varying degrees of inflammatory reaction and beginning interstitial proliferation. The myocardial abnormalities could be compared with lesions observed in the human heart in moderate or severe diphtheritic toxemia. As far as relation to irradiation was concerned, Warthin and Pohle found that interpretation of the lesions was rendered difficult by the catarrhal or purulent bronchitis and bronchopneumonia which were common complications; these affected especially the main bronchial trunks and the portions of the lungs in the anterior mediastinum, and their severity varied from catarrhal bronchopneumonia to multiple pulmonary abscesses. Local or generalized mediastinitis, pleuritis and pericarditis also were present. Among both the irradiated and control animals bronchial and pulmonary infection was almost universal. It seemed probable that this began in the irradiated animals, but reasons for this assumption were not given. "As the result of the irradiation, the bronchi are damaged, the resistance lowered, and an infective bronchitis and bronchopneumonia developed. This in turn will increase the damage already produced by the irradiation in the myocardium." The fact that the controls were kept with the irradiated animals was thought to favor the spread of infection. It was held that precordial irradiation injured the main bronchi to such a degree that pulmonary infection generally resulted, that to primary myocardial injury was added the possibility of increased toxic injury and mechanical strain, that secondary infection may extend directly to the pericardium and heart, or that the latter may become involved through hematogenous infection of the endocardium. In two rabbits there was also thrombo-endocarditis. Colonies of bacteria in all the lesions proved their infective nature. "Unfortunately, similar pulmonary lesions were found in the majority of the controls, and in some of these the same type of myocardial lesions of a less severe degree." In addition to pulmonary infection, three animals had myocardial lesions similar to those commonly found in encephalitis of rabbits. Because some of the rats and rabbits had milder lesions in spite of associated pulmonary involvement, and because the control animals with bronchopneumonia usually presented milder lesions of the myocardium, Warthin and Pohle thought it safe to conclude that the heart lesions were due in large measure to irradiation. Because of the complicating cardiac lesions of rabbit encephalitis this deduction seemed safer as applying to the rats than to the rabbits. Rabbits, therefore, were regarded as unsuitable for such investigation.

The mediastinal lymph nodes and thymus gland gave evidence of lymphoid destruction and hyperplasia of reticulo-endothelial cells; areas of fat necrosis were seen in the mediastinal fat, and the ganglions in the exposed region showed chromatolysis and lipoidosis. Many nerve trunks were edematous, and some also showed lipoidosis. Some of these lesions occurred only in the irradiated animals and were not related to the pneumonia or due to infection. Warthin and Pohle felt justified in assuming that irradiation produced a primary injury to the heart, large bronchi, portions of the lungs, lymph nodes, thymus and ganglions, with secondary infective bronchitis and bronchopneumonia, frequently extending to the pleura, mediastinum and pericardium, and associated in two cases with hematogenous bacterial thrombo-endocarditis. Pathologic changes common to infection were usually more pronounced in the irradiated animals than in the controls that died from severe pulmonary infection.

Although direct comparison of their results with those obtained by Hartman, Bolliger, Doub, and Smith was impossible, and in spite of the fact that the smallest dose used by the latter was estimated as a multiple of the dose used by themselves, Warthin and Pohle confirmed their conclusion as to the possibility of injury to the myocardium by roentgen rays of short wave-length. They added that "as far as our own clinical experience is concerned, no roentgen-ray injury of the heart was observed at autopsy in patients who had been treated over the precordium." And they concluded that multiple exposures of the precor-

dium to roentgen rays caused definite injury to the myocardium, that the myocardial lesions in the irradiated animals were always associated with more or less severe bronchitis, bronchopneumonia, and evidence of roentgen injury to the thymus, mediastinal lymph nodes and ganglions, and that the pulmonary infection was secondary to radiation injury to the bronchi and to a resulting loss of resistance.

(*To be continued*)